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INFECTION IN INFANCY *

BY

ROBERT CRUICKSHANK, M.D., M.R.C.P., D.P.H.

Pathologist, L.C.C. Group Laboratory, North Western Hospital, Hampstead

I have chosen as my text ' Infection in Infancy ' because I believe that paediatricians have a duty (1) to teach students and practitioners to regard the infant not as a ' miniature man ' but as a creature with its own and often inadequate way of reacting to infection, and (2) to impress upon a larger public that infection in infancy is closely correlated with malnutrition and poor environment.

It is customary to divide infant mortality into deaths in the first month (neonatal mortality) and deaths between the first month and the first year of life. Neonatal deaths, which constitute more than half of the infant mortality, are mostly attributable, directly or indirectly, to prematurity, with congenital defects and bad obstetrics as additional contributory causes; the bulk of them occur in the first week of life. Death from infection, apart from post-asphyxial and aspiration pneumonia, is relatively unimportant at this early stage, and it might be wiser to combine deaths in the first week with the still-birth rate, for their causes are similar and their prevention is closely linked with better nutrition and supervision of the pregnant woman. Although this is not primarily the responsibility of the paediatrician, he will share in the general satisfaction at the remarkable reduction in the still-birth rate and neonatal mortality during the war years. Still-births have fallen from 36 per 1000 in 1940 to 28 per 1000 in 1944 and neonatal mortality from 29·6 to 24·5 per 1000, an astonishing achievement which must be directly related to the better nutrition of the pregnant women and is to be regarded as one of the major victories of the war.

* The George Frederic Still Memorial Lecture delivered before the British Paediatric Association at Rugby on August 3rd, 1945.

The infant's reaction to infection

The first and outstanding feature of infection in infancy particularly in the first six months of life, is that it is mostly due to endogenous bacteria; that is, bacteria which ordinarily live as saprophytes in the upper respiratory tract, in the bowel or on the skin, and which in older children and adults have little power to initiate infection. Chief among these are certain pneumococcus types (e.g. types 4, 6, 19, 23), the coliform family, the staphylococci and monilia. These bacteria may be transferred from one child to another, and induce infection if dosage is large and resistance is low. The preponderance of a particular pneumococcus type, e.g. type 19, in broncho-pneumonia (Hendry, 1942) or of a coliform organism, e.g. Bact. coli neapolitanum in infantile enteritis (Bray, 1945) can be explained on this basis. By contrast, the exogenous infections (scarlet fever and other streptococcal infections, diphtheria, measles, tuberculosis, even the common cold) are relatively rare although these are all air-borne diseases to which the infant is often exposed. The specific intestinal infections are also uncommon in infancy and only pertussis seems able to break through the early barrier with any frequency.

Defective defences. Endogenous infection in the early months of life is closely associated with overcrowding and poverty, for it is much less frequent in the highest than in the lowest social classes but, given adverse conditions, the occurrence of infection is facilitated by the poor response which the infant's tissues make to invading bacteria of low virulence. This poor response is probably related to the immaturity of the defence mechanism. When older tissues are attacked, there is an immediate outpouring of

TABLE I

DEATHS IN CHILDREN AGED 0 TO 5 YEARS; 1938

AGE	Months		Years				
	0–6	6–12	1	2	3	4–5	0–5
Pneumonia	2,943	1,961	1,581	514	286	167	7,452
Enteritis	2,129	891	275	59	36	24	3,414
Tuberculosis	118	258	414	264	196	127	1,377
Measles	65	327	538	235	136	88	1,389
Whooping cough	281	268	323	95	76	29	1,072
Diphtheria	25	48	107	215	296	320	1,011
Scarlet fever	2	8	26	46	25	49	156

phagocytes—both polymorphonuclear leucocytes and mononuclear or macrophages—followed in a few days by the appearance of humoral antibodies, and the infection is localized and overcome. But the production of phagocytes and antibodies requires efficient factories and the necessary raw material, both of which are inadequately provided by the infant. Thus its leucocytic response contains many immature white cells, and experiment has shown, as indeed is known from the infections that accompany leukaemia, that these immature white cells are poorly equipped to deal with invading bacteria. Macrophages are derived, according to Maximov, from the lymphocyte but lymphoid tissue is poorly developed in the infant at birth and the germinal centres or factories do not become prominent until some months later. The excess of lymphocytes in infant blood probably reflects the constant demand on the lymphoid system to produce these cells and the lymphoid hyperplasia in the early years of life is evidence of the child's response to the many foreign stimuli it receives. Thus enlarged tonsils and adenoids are to be regarded as part of the defence mechanism rather than a menace to health, and it is a sad commentary on medicine that tonsillectomy is, or has been, four times more common among well-to-do than among poor-class children (Glover and Wilson, 1932). Experimental work lends support to the view that lymphoid tissue reacts to bacterial stimuli. Thus guinea-pigs reared in an aseptic atmosphere so that they did not acquire the usual endogenous bacterial flora throve well, but their lymphoid tissue failed to develop normally and there was a complete absence of germinal centres. Young rabbits, injected intravenously with killed bacterial vaccines, showed a rapid and marked development of germ centres in spleen and lymphatic glands.

Lymphoid tissue may also be a main source of antibodies, for after the local injection of viruses or bacteria in rabbits the regional lymph gland and the efferent lymphatics were found to contain a higher concentration of antibody than the blood (Ehrich and Harris, 1942). More recently, the lymphocytes themselves in the efferent lymph vessels have been found to contain four to eight times the concentration of antibody found in the plasma and this was not due to adsorption of the antibody on to the lymphocytes (Harris et al., 1945). Antibodies are mostly concentrated in that part of the plasma protein which is now known as gamma globulin. The plasma protein level is mostly low in the newborn (usually 4 to 6 gm. per cent.) and particularly so in premature babies (3·7 to 5·4 gm. per cent.) (Hickmans et al., 1943) but detailed analysis has not yet been made of the composition of the infant's plasma proteins. In the newborn calf the globulin content is very low but the calf acquires maternal antibody after birth from the colostrum, whereas the transfer of human antibody is mostly via the placenta and is already in the infant's blood at birth. If, however, an abundant supply of natural antibody should help the infant to cope with endogenous as well as exogenous infections, concentrated gamma globulin is now available and might well be tried in the treatment of bronchopneumonia and gastro-enteritis.

The lack of reactivity of the infant's tissues helps to explain the anomalous clinical infections seen in infancy: staphylococcal osteomyelitis with little or no localizing signs; staphylococcal pneumonia; coliform infections of lungs and meninges in the first few weeks of life; severe and even fatal monilia infections; fulminating pneumococcal septicaemia detected only by bacteriological examination post-mortem. Fortunately the pioneer work of MacGregor (1943) on the etiology and pathology of infantile infection is now being followed in other centres, and the prudent paediatrician is learning to correlate what were puzzling clinical phenomena with the pathological findings. The infant's poor response to infection also helps to explain disappointing results obtained with the new chemotherapies. Anderson's (1943) comparison of deaths from pneumonia in Glasgow in the sulphonamide and pre-sulphonamide periods has shown how important is the host's reaction in overcoming bacterial infection. Thus while deaths from pneumonia in the age-group 10 to 45 during the years 1939–41 were only 40 per cent. of those of the presulphonamide era (1922–38), deaths in infants under one year of age were still 75 per cent. of those of the earlier period and the reduction could probably be ascribed as much to social improvement as to sulphonamide-therapy. As an example of the relative failure of sulphonamides in early infancy, Professor G. B. Fleming has allowed me to quote a case mortality of 48 per cent. among 100 infants under six months of age admitted with primary pneumonia to the Royal Hospital for Sick Children, Glasgow, during the past three years. It will be interesting to see if penicillin-therapy greatly alters this figure.

Immature physiology. Besides the poor response of the defence mechanism to infection the infant physiology is also unstable and immature, and its dysfunction may quickly lead to irreparable damage. It might therefore be profitable if more attention were given to physiological upsets in the respiratory and alimentary systems and in the blood-chemistry as a result of infection, and attempts were made to correct these upsets early rather than late. Thus the baby with respiratory and other infection seems prone to anoxaemia, and oxygen therapy, perhaps combined with helium to help diffusion, should be used earlier and more liberally than it is in many paediatric units; the pathology of the brain of infants dead of infection also needs intensive study. Again, in intestinal infections the inadequacy of the infant's physiological response is obvious. As Miller's (1942) studies have shown, gastric acidity is low in the early months of life and gradually reaches adult level about the end of the first year. The artificially-fed infant drinking contaminated milk is therefore poorly protected against the introduction of foreign bacteria into the bowel, particularly as, in addition, cow's milk

protein makes greater demands than human milk on its gastric juices. Pyrexia also reduces gastric acidity. The inadequacy of the acid barrier allows colonization of the normally sterile upper reaches of the small intestine with irritating effects on a gut which at the best is none too stable. This intestinal upset may be accompanied by absorption of toxic products to the liver via the portal system with resultant dysfunction of another vital organ. In a series of 31 autopsies on infants with enteritis at the L.C.C. North Western hospital, two-thirds of the cases showed varying degrees of liver damage, compatible with a toxaemia. In a larger series of 100 cases at the Hospital for Sick Children, Great Ormond Street, 71 per cent. showed fatty change which was extensive in 39 per cent. whereas in a control series of similar age, 59 per cent. showed fatty change which was severe in only 18 per cent. of the cases (R. Stern: unpublished observations). In this connexion Gale (1944) found that certain enterococci which were prevalent in outbreaks of neonatal diarrhoea had a high activity in converting tyrosine to tyramine, an amine which is toxic to young rats and probably also to babies who have not yet developed the appropriate detoxicating enzyme. My colleague, Mrs. Tomlinson, has followed up this promising line of research by examining the enzymic activities of a large series of coliform bacilli from infants with enteritis and from normal controls but so far has failed to discover anything comparable to the enterococcus enzyme. Again, in the treatment of infantile enteritis, the first necessity is to relieve dehydration, and the older practice was to give the infant liberal amounts of normal saline or glucose saline intraperitoneally or intravenously. However, the work of Young and McCance (1941, 1942) has shown that the infant kidney has a poor capacity for eliminating sodium so that a large addition of salt to the baby's tissues only results in oedema. The hydrating fluid should therefore contain the minimum of sodium consistent with the correction of acidosis from loss of base from the bowel, and a mixture which serves the purpose well is half-strength Hartman solution plus 5 per cent. glucose. As important as hydration is the treatment of shock from which so many infants with gastro-enteritis suffer in varying degree. In such cases half-strength serum or plasma intravenously should follow and alternate with the Hartman solution, and this anti-shock treatment has been of the greatest value in saving the lives of infants with gastro-enteritis. Thus in a series of sixty-nine dehydrated babies treated in this way by Alexander and Eiser (1944) at the North Western Hospital, the fatality-rate was 11·6 per cent. which may be contrasted with a more usual figure around 50 per cent.

I have avoided direct discussion of the etiology of infantile enteritis, but, if it is remembered that this puzzling infection occurs principally among artificially fed infants in poor class urban communities and has its greatest incidence and mortality in the early months of life, my thesis that these early infections are associated with endogenous bacteria would force us to cast strong suspicion on the intestinal group of organisms. The recent summer epidemics in Glasgow and Dublin lend support to the view that contaminated milk may be a precipitating factor for hygienic standards have been lower and flies more prevalent in the war years. A comprehensive study of the rather analogous infection, scours in calves, would probably help in elucidating the etiology of infantile enteritis, and I am glad to say that the Agricultural Research Committee is undertaking such a study.

Infection and nutrition

I want next to consider how far infection in infancy is related to deficiences, both qualitative and quantitative, in the diet. The close association between malnutrition and infection is well known, but morbidity and mortality rates are apt to be confused. Thus exogenous infections like measles and pertussis are as common among well-fed as among ill-fed children; yet in the age-group one to two years deaths from measles are eighteen times more common in the lowest than in the highest social class. Susceptibility is the same but resistance to established infection is for a variety of reasons very different. Although strictly comparable data on the relative susceptibility to endogenous infection of well-nourished and malnourished children are difficult to obtain, we know that certain deficiencies, more prevalent among the poor, predispose to infection; thus inadequate intake of the more common vitamins makes tissues more susceptible to infections by affecting epithelial surfaces, muscle tone, intercellular cement or bony structure; but there is no evidence that excess of vitamins gives added resistance. Lack of iron and the consequent secondary anaemia, still all too common, also predisposes to infection as Mackay's (1931) studies showed.

We are on surer ground in stating that the underweight child has a poor resistance to established infection, although we cannot surely say why. Thus among 235 children under two years of age admitted to the Royal Hospital for Sick Children, Glasgow, with primary pneumonia the fatality-rate in 181 moderately or well-nourished infants was 39·2 per cent. compared with 72·2 per cent. among 54 poorly nourished children (Cruickshank, 1933). Malnutrition is common among hospital admissions; Graham (1944) found that two-thirds of 295 children admitted to the Royal Hospital for Sick Children, Glasgow, in 1940–41 were under 90 per cent. of their expected weight and one-fifth were less than 70 per cent. of normal. The fatality-rates were 20 per cent. among children over 70 per cent. of normal and 43·5 per cent. in the definitely underfed children. This poor resistance of the under-weight child to established infection is a complex affair which only animal study is likely to unravel. Some progress has been made on the protective value of protein, a deficiency of which is probably the commonest cause of malnutrition in the infant. Rabbits on prolonged protein

restriction lose the power to produce antibodies and consequently to combat infection, a finding that may have a bearing on attempts to immunize malnourished children in Europe against diphtheria. Again, in a carefully controlled study with pure line mice, Watson (1937) found that a diet which included milk casein greatly increased the animal's resistance to mouse-typhoid, so that skimmed milk may not be an ' unsuitable food for babies ' in spite of the label on the tin. Protein restriction also leads to anaemia in animals since haemoglobin is a compound of iron and protein, and my colleague Dr. Gillespie has lately collaborated in an investigation with young rats fed on a lysine-free diet which resulted in anaemia and hypoproteinaemia probably due to a reduction in the labile protein store in the liver. It may be that some of the refractory anaemias in infants and pregnant women will only respond when an adequate diet is prescribed. Anaemia and hypoproteinaemia are common in infants with enteritis, and it therefore seemed rational to try to correct this deficiency and so raise the child's resistance to intercurrent infection by giving it readily utilizable protein in the form of casein hydrolysate. We have been experimenting at the L.C.C. North Eastern Hospital with these amino-acid concentrates, and preliminary trials suggest that when used as supplements to the diluted milk feeds as soon as the diarrhoea ceases, they are acceptable to the infant and hasten convalescence.

Breast versus artificial feeding

No discussion of the effect of nutrition on infantile infection can avoid analysis of the relative merits of breast and artificial feeding. The merits of breast feeding are rightly pressed but it should be noted that the decline in infant mortality in the past twenty years has been accompanied by a decreased rather than an increased incidence of breast feeding. If, however, the incidence of infection among naturally and artificially fed babies is compared, some striking differences emerge. Grulee and his colleagues (1934) in a survey of over 20,000 infants reported morbidity rates of 37·4 per cent. among wholly breast-fed babies, 53·8 per cent. among those breast fed for a short period, and 63·6 per cent. among wholly artificially-fed babies. In Toronto, among 1500 babies under one year of age admitted to the Children's Hospital with various infections (about three-quarters of them respiratory) only 15·1 per cent. were wholly breast fed, 29·1 per cent. had been breast fed for at least six weeks and 55·7 per cent. were artificially fed from birth (Ebbs and Mulligan, 1942). In comparison, the feeding histories of babies attending welfare clinics were 35·6 per cent. wholly breast fed, 36·2 per cent. partially breast fed and 28·1 per cent. artificially fed. Again in a small group of 54 infants aged one to four months admitted to the Royal Hospital for Sick Children, Glasgow, with primary pneumonia, there were three deaths among thirteen wholly breast-fed cases and 22 deaths among 41 artificially fed or partially breast fed. There were no breast fed babies among 24 such cases aged four to six months (Fleming, personal communication).

The close association between gastro-enteritis and artificial feeding is well known but a more detailed analysis of the feeding histories of infants with enteritis provides some interesting data. Gairdner (1945) found that among artificially-fed infants the case-mortality from enteritis was 55 per cent. in 60 cases breast fed for less than one month (but over one month of age on admission) whilst it was only 28 per cent. in 39 babies breast fed for one month or more. Smellie (1939) also reported a fatality rate of 25·9 per cent. among infants with enteritis who had been breast fed for a month or more compared with 70·6 per cent. among infants who had never been breast fed. These are striking figures and immediately suggest that breast feeding for even a few weeks gives the infant some added protection against infection. What is the explanation? Is antibody transferred from mother to infant in the colostrum and milk? In lambs and calves, ingestion of the colostrum provides protection against lamb dysentery and calf-scours, but in these animals antibody cannot pass through the placenta because of the several layers between maternal and foetal circulations. In the human the bathing of the chorionic villi in the maternal blood-sinuses allows natural antibody to pass freely from mother to foetus and this is the main route for the passive transfer of maternal antibody. Human colostrum contains much lower concentrations of diphtheria antitoxin than does the blood, and milk none at all, while there is no demonstrable increase in the antitoxin level of infant's blood as a result of colostrum feeding (Kuttner and Ratner, 1923). Experiments with rabbits which have a similar placental structure have also yielded negative results on the transmission of antibody via the milk, yet Gröer and Kassowitz (1919) claimed that passive immunity to diphtheria was maintained far longer in breast-fed than in artificially-fed infants. The whole problem needs further investigation both experimentally and clinically.

Breast milk is a natural food and, if present in sufficient amount, should satisfy the infant's requirements for a properly balanced diet. The baby who continues to thrive on the breast is presumably getting most of what it needs although more data are needed on human milk analyses including vitamin-content. It is certainly remarkable that deficiency diseases like rickets, scurvy and nutritional anaemia are rare or mild in breast-fed babies, and the possibility that the appropriate minerals and vitamins, although present in smaller amount in human than in cow's milk, are more completely absorbed from the gut of the breast-fed baby needs examination. Human curd is more digestible and probably more completely broken down than cow curd, and the reaction of the breast-fed baby's faeces with its homogeneous aciduric flora is much more acid (pH around 5·0) than that of the artificially-fed child which has a mixed bacterial flora and

a neutral or alkaline stool like that of the adult. Perhaps this more acid reaction favours the absorption of calcium phosphate, iron and vitamins and explains the frequent failure to cure deficiency diseases by vitamin supplements given by mouth to the artificially-fed child.

An impartial analysis of the data available would probably justify the view that in the present social conditions breast feeding by 80 per cent. of mothers for six months would materially reduce both morbidity and mortality rates in infancy. This objective is perhaps more readily attainable than is generally believed. Apart from the maladjustments in the early weeks, the majority of mothers cease to feed their babies because lactation fails for no obvious reason or because of preventible breast infections or general debility (Robinson, 1939, 1941, 1942). Both animal and human studies indicate that continued lactation is largely dependent on adequate nutrition during pregnancy and throughout the feeding period. Thus Mackintosh (1943) in Aberdeen was able to report that of 200 women confined in a private nursing home 80 per cent. compared with only 29 per cent. of a similar number of mothers in a poor class district were still breast feeding their babies at six months. In Canada improvements in the diet of low-income women allowed an additional 15 per cent. to continue feeding their babies for six months (Ebbs and Kelley, 1942).

Infection and environment

Every analysis of infant mortality shows how closely high death-rates are correlated with poor social conditions. It is difficult to disentangle the adverse environmental factors—overcrowding, bad housing, poor hygiene and way of life—which contribute to infant morbidity and mortality from infection. Such studies as those of Titmus (1943), the Wrights (1942) and the Scottish Report should be read more widely by medical men, for the remedies will be accelerated by all the publicity that can be given to the facts of the case. Our particular concern was pungently put by Florence Nightingale eighty years ago when she wrote that the first requirement in a hospital is that it should do the sick no harm. If residential and day nurseries are included in the term hospital, it is obvious that this requirement is still far from being satisfied. Cross infection becomes a serious problem wherever young children, whether sick or healthy, are brought together. Fortunately there is an increasing consciousness that infants under one year of age should not be admitted to hospital unless they can be nursed in individual rooms and, if the child is under six months, efforts should be made to accommodate the mother as well. The recently published experience of the Pickerells (1945) is convincing. In a suburban house converted to a nursing home to accommodate twelve mothers and children, they had no case of secondary infection in a three-year experience of the surgical treatment of congenital defects like hare-lip, cleft palate and hypospadias. The remarkable figures from the Cradle for Foundlings at Evanston where the infant case-mortality was reduced from 5·8 per cent. to 0·8 per cent. bear tribute to the value of a rigid isolation and antiseptic technique (Sauer, 1935). Nearer home, the post-operative mortality among babies with pyloric stenosis was reduced from 9 per cent. to less than 1 per cent. at the Hospital for Sick Children, Great Ormond Street, after the new hospital was built and more isolation accommodation became available. Even the strict technique of barrier nursing which is practised in fever hospitals is not enough, for among cases of gastro-enteritis admitted to the North Western Hospital the relapse rate in the barrier ward was four times that in the isolation ward where babies were nursed in single-bedded rooms (Alexander and Eiser, 1944).

For cross infections due to exogenous pathogens like the haemolytic streptococcus, the new technique of oiling floors and blankets will greatly reduce the risks, particularly where the load of infection is high and the respiratory mucosa very susceptible as in measles wards (Wright, Cruickshank and Gunn, 1944). The use of aerial disinfectants such as ultra-violet light or chemical substances which are vaporized into the air, will probably prove beneficial in controlling the spread of respiratory virus infections like the common cold and influenza. Thus in a convalescent children's home for long-stay patients Harris and Stokes (1945) reported a ratio of 1:10 of upper respiratory infections in the wards treated with vaporized glycol compared with the control wards. Improved hospital design and equipment in conjunction with an adequate and properly trained nursing staff are, however, the most important requirement to protect the infant against infection. The recent experience of Jacoby (1944) in a unit of 33 beds consisting of an isolation unit of five single rooms and four single-bedded, two two-bedded, four four-bedded and one six-bedded wardlets shows what can be accomplished, for in a year's turnover there were only three instances of secondary infection among 74 infants under 18 months while the cross-infection rate among the older children in the small wards was 6 per cent. Advice about the sources, modes of spread and methods of control of infection in hospital is given in the Medical Research Council's War Memorandum, No. 11. Although improved isolation accommodation and better equipment are sorely needed in most hospitals, much could be accomplished if each hospital had its own cross-infection committee composed of clinicians, nurses and bacteriologist to overhaul the existing machinery and to devise practicable and effective procedures for dealing with incidents such as a case of diphtheria or scarlet fever or measles or Sonne dysentery in an open ward. Nurses should also be given a short course in applied bacteriology early in their training so that they can intelligently carry out the ritual which is needed if our hospitals are to do the sick no harm.

Residential and day nurseries need expert super-

vision, and both the paediatrician and the bacteriologist should be co-opted to handle the problem of infection which can do so much harm among young children in nurseries. Residential nurseries are, I suppose, required in any large town but large wards or rooms should be banned, and admission of infants under one year of age should not be made easy. The unique experience in the Greater London area of a rising mortality rate from gastro-enteritis may be partly attributable to the necessity to provide residential accommodation for a large number of young children (Gairdner, 1945). The unwanted illegitimate child illustrates well the hazards that attend the infant deprived of parental care. For example, the illegitimate London child has a 1 in 40 chance of dying of diarrhoea before it reaches its first birthday. Yet Birmingham has shown that, by proper supervision of these unfortunates, their mortality rate can be reduced to a lower level than that of legitimate children.

In the day nursery exogenous infections like measles, whooping cough and Sonne dysentery are responsible for much of the sickness, and methods of controlling these infections in semi-closed communities are now available in the use of convalescent measles serum or gamma globulin, pertussis vaccine and antiserum and chemoprophylaxis. Great benefit would follow if the age of attack of infections like measles could be postponed, for two-thirds of the deaths from this disease occur between six months and two years of age. The childhood fevers are mostly brought into the home from school, and an interesting investigation in Philadelphia suggests that epidemic spread of measles and chicken-pox among children in school can be largely controlled by continuous irradiation of the classrooms with ultra-violet light through the winter months (Wells, Wells and Wilder, 1942). If so, the age of attack could be postponed and children could have their attack of measles when it is least likely to do them harm.

If I may close in a critical mood, I would say that in the past the paediatrician has been too much concerned with infection in the individual child and not enough with infection in the child community. With chairs of child health being established in almost every University city, there will be many opportunities to correct this fault if and where it exists. I have tried to indicate some of the problems that need to be tackled both in the individual infant and in the community and I can only hope that George Frederic Still would have nodded approval of my effort. In the words of Alva Myrdal: ' As soon as the economic machinery has been repaired in a provisionary way so that international exchange is again functioning and the masses of workers are given employment and bread, a new interest will attach to productive investment in a nation's chief economic asset: children and their health and capabilities.'

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THE CLINICAL MATERIAL OF HEALTH IN PAEDIATRICS

WHERE TO GET IT, AND HOW TO USE IT

BY

CHARLES McNEIL, M.A., M.D., F.R.C.P.Ed., F.R.C.P.

Professor of Child Life and Health, University of Edinburgh

In the reports of the Goodenough Committee on Medical Schools, and of the Paediatric Committee of the Royal College of Physicians of London the teaching and study of paediatrics have been carefully considered. In both reports the subject has been divided into the study of health and of disease; and it is agreed that the study of health as regards clinical teaching has been neglected in the medical schools, and proposals are made for getting access to the clinical material of healthy infants and children. Both reports make definite and generally similar proposals that this clinical material of health, hitherto lacking, should be found in newborn nurseries, in child welfare centres and in school clinics. It is the purpose of this communication to examine the teaching and study of child health as a part of paediatrics and to suggest a change in the proposals made in these two important reports.

There is no difficulty in getting the clinical material of disease in children. This is already provided in convenient and large concentrations of cases of disease in children's hospitals. But under present conditions the clinical material of health lies scattered about and dispersed both in time and space—the first few days of life in maternity hospitals, the succeeding months and years in welfare centres and school clinics: and it is recommended that teachers and students should go out and follow these pockets of clinical material from place to place and from age to age. This no doubt will improve the teaching of child health: but it falls far short of the opportunities opened up by this new field of clinical study.

Principles of study of disease and health

Let us examine the two subjects of study in paediatrics—disease and health. In any disease, we study some part of child life (body or mind) which is at fault; make an intensive examination of the faulty part; and apply the remedy, taking into account also the effect of the disease on the whole life of the child. And we use the same general method in all kinds of diseases.

In the study of health we examine the whole life-state (soma and psyche) and investigate the agents or factors, both physical and metaphysical, that are necessary to maintain life at the level of health, trying to discover and correct any deficiencies in the standards of health, or in the agents of health. And this double examination must be made again and again throughout the period of childhood, since in the course of growth changes are continually taking place, both in the physical and psychical states of life, and also in the agencies that sustain healthy life. So that for the proper study of health in a child, the physician requires a continuity of observation in the same individual child from birth, and should have this clinical experience repeated in a number of children.

In the study of disease, we study pathology in a great number of separate pathological problems; and the more examples of each kind, the richer is our clinical experience of disease in children.

In the study of child health, we study the whole life, physiology, anatomy and psychology in continuous variation from birth to puberty; and the more cases of such life studies we carry out, the better are we qualified to teach and practice child health. Fig. 1 gives a scheme which may help to illustrate in a single child this rather abstract exposition of the study of child health.

A single central health clinic. If this is a sound argument, the suggested arrangements for the study and teaching of child health in different units fail to provide, either for the teacher or the student, a connected view of the problem of growth and development. But this continuity can be provided by keeping under observation, examination, supervision and record the newborn babies in a teaching maternity hospital, and on discharge in a follow-up clinic attached to the hospital, periodic examinations being conducted on this same group throughout the years of infancy and childhood. Here in a single large child clinic there will be living examples of the health problems at every stage of growth, and in each child a record of his development from birth and also of the incidents of illness that have occurred in his life. If such a single unit of healthy children were created, organized, equipped with facilities for study and teaching, and properly staffed, the medical school would then have the clinical material of disease in the single large unit of a children's

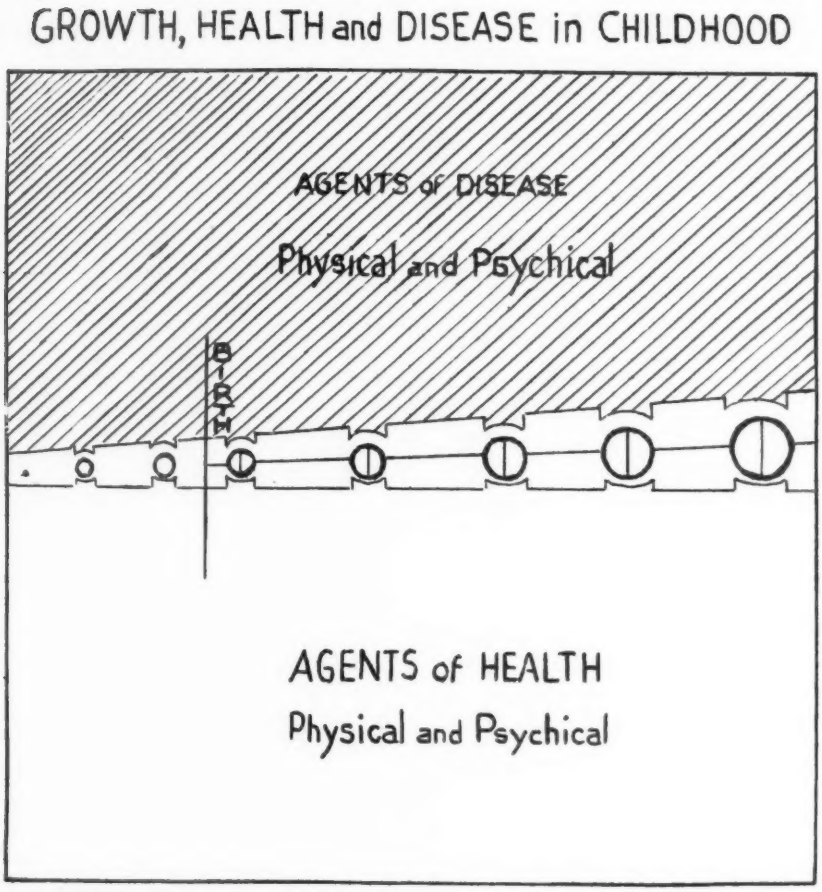

FIG. 1 illustrates the continuity of study of child life in one individual between birth and puberty: showing five stages or ages, in each of which the sphere of life is divided into the hemispheres of soma and psyche: and the factors or agents, physical and psychical, sustaining health in the progress of life, and those of disease threatening it.

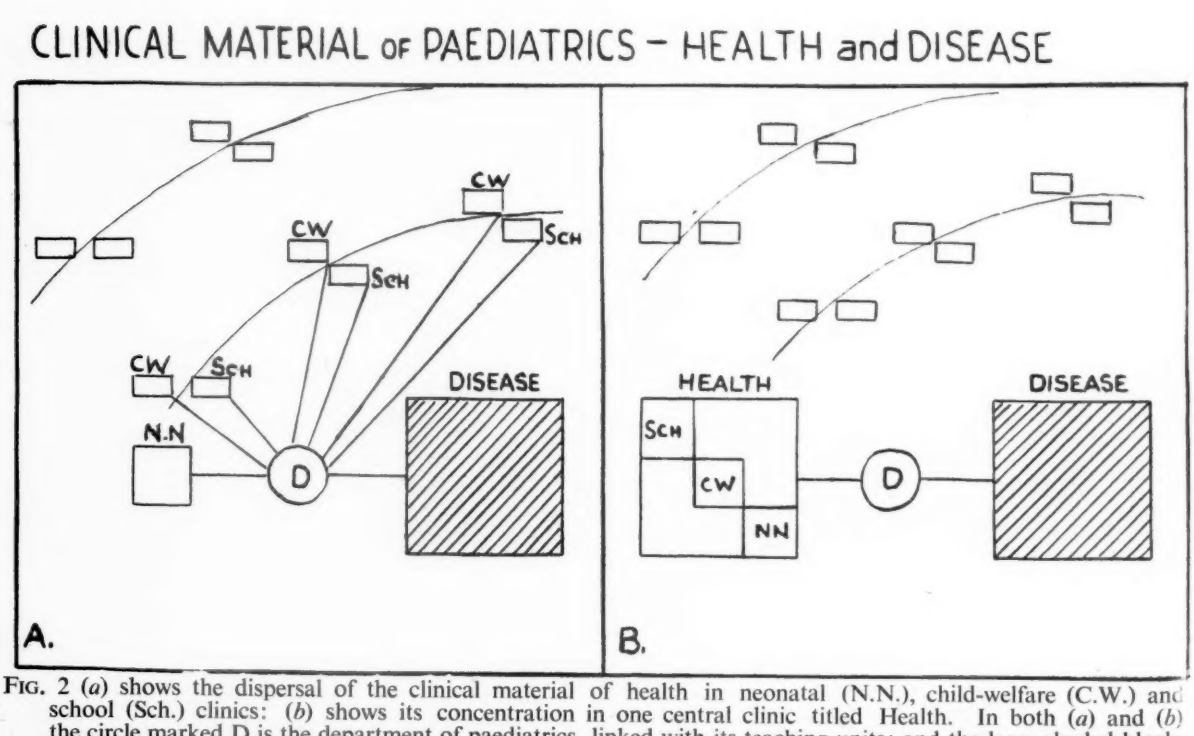

FIG. 2 (*a*) shows the dispersal of the clinical material of health in neonatal (N.N.), child-welfare (C.W.) and school (Sch.) clinics: (*b*) shows its concentration in one central clinic titled Health. In both (*a*) and (*b*) the circle marked D is the department of paediatrics, linked with its teaching units; and the large shaded block, titled Disease, is a children's hospital.

hospital, and the material of health in a single large health clinic, with the paediatric department of the school conveniently placed between them.

This proposal of one central health clinic for children is put forward for the consideration of those who are now planning new departments of child medicine or are reorganizing and extending departments already in existence. It should be examined alongside the different arrangements for the teaching of child health set out in the Goodenough and the Royal College of Physicians Reports. The two diagrams in fig. 2 illustrate in a simple way the two alternatives.

Organization of the child health clinic

STAFF. The composition of the staff of this single central health clinic is important. It should consist of hospital paediatricians, and of experienced child welfare and school medical officers. These members of the local authority medical service ought to be full partners in the work of the clinic, taking an active part in teaching, study and investigation; and they should receive appropriate titles in the medical school. This joint staffing would be a just recognition of the established position of the local authorities' health services for children, and of the unique clinical experience of their medical officers in this field of practice: and it would go a long way to secure that integration of the work of hospital paediatricians and public health doctors which has been recommended in the National Medical Service White Paper and in the Orr Report on Infant Mortality. A place on the staff should also be found for the family doctor who handles the problem of child health at its centre in the home.

The non-medical staff should consist of capable and experienced health visitors and of midwives. It should also include a nurse specially trained in breast-feeding and infant dietetics, a dietitian for the mothers and older children, and an almoner.

TEACHING. Such a clinic would be a training school for all those who are or will be responsible for the care of infants and children. The first are the mothers; and so long as they attend, they will receive authoritative guidance and instruction in the care of their own children. Next are the medical students, who will become family doctors: then pupil health visitors; pupil midwives; and post-graduates in training as specialists in child medicine and social medicine. The clinic would also serve as a training school for the medical and nursing members of the local health services who could attend and take part in the administration and work of the clinic.

RESEARCH. The field of research opened up by such a well-staffed clinic is rich and wide—child physiology, psychology and anatomy; and that part of social medicine that deals with the life and health of the human family. Research and investigation beginning in the clinic would go out of it and into the home; studying the child in the clinic, and the physical and spiritual environment of the child in the home.

An experimental child health clinic.

There is a natural and reasonable distrust of airy schemes of theory without practice. What has been written in this article is largely theory; but a small beginning has been made in putting the theory into practice. In the medical school of the University of Edinburgh, a child health clinic was established in 1929 at the old Maternity Hospital, its clinical material being the newborn babies in the hospital, and later attending the follow-up clinic during the first year of life. In 1939 the old hospital was transferred to the new Maternity Pavilion of the Royal Infirmary; and with larger premises and increased staff, extension of the work of the clinic in teaching and research took place. The difficulties of the war and the withdrawal of members of the staff have prevented full development, and the clinical material is still confined to the first year of life. The staff of the clinic now consists of three hospital paediatricians, and an associate paediatrician in the person of the senior child welfare officer of Edinburgh Corporation. Lately the Nuffield Trust has provided the salary of a Sister-Midwife who is now being trained in breast-feeding and infant dietetics. An almoner regularly attends the sessions of the clinic which are held thrice a week with 6000 annual attendances. In the nurseries there are about 3000 births a year.

TEACHING. In the teaching of medical students, a clinical course of eighteen meetings in each academic term is given, eight being devoted almost entirely to the health problems of the first month (clinical examinations and records, breast-feeding, prematurity and counter-infection), and ten meetings on the health problems of the remainder of the first year. This clinical teaching follows a standardized programme of subjects, dealt with in a regular sequence; and the teachers follow agreed methods of examination and agreed principles and practice of infant dietetics. In this way the practice of child health, limited to the first year of life, is taught to about 200 students a year, this aggregate divided into three separate groups of 70, and each group subdivided into sections, receiving its clinical instruction in these eighteen meetings. This clinical teaching is strictly correlated with systematic lectures on child health given to the whole ' year ' of 200 students.

The clinic is also responsible for the paediatric teaching of pupil midwives, and takes a small part in the teaching of pupil health visitors.

RECORDS. Effort has been made by carefully designed record-sheets and by the use of abbreviations and symbols, to keep sufficiently full and accurate and continuous records from birth throughout the first year of life.

RESEARCH. Meantime research has been mainly confined to the neonatal period. A pathologist specially trained in child pathology is an important member of the staff, and statistical and pathological studies on neonatal problems have been and are being carried out. But some attention has also been given to physiological problems of the first month. One of the paediatricians also acts as registrar of clinical and pathological records and

each year makes a careful analysis of hospital vital statistics of the neonatal period.

In these ways there has been a try-out of the theory of a single central health clinic for children in a large medical school, as a complement to the hospital clinic for diseases of children. It is only a beginning. But it begins at the beginning; and from birth, it deals month by month in unbroken continuity with the first year of life. On this foundation the structure of a complete clinic of child health can be built up. I believe it to be a better way of dealing with the problem of research and teaching in child health than that proposed in the reports of the Goodenough and Royal College of Physicians Committees.

Summary

An outline is given of a plan to concentrate in a single clinic, based on a maternity hospital, the complete clinical material of child health, for the purposes of teaching and research in a medical school.

A short account is given of the experimental trial of such a clinic, of its structure, staffing, and operation in teaching and research.

THE NATURE OF STILL'S DISEASE

WITH REPORT OF A CASE

BY

F. A. LANGLEY, M.Sc., M.B., Ch.B.

(From the Department of Pathology, Victoria University of Manchester)

The following case of Still's disease is reported because of the unusually full pathological data that were available and because of the light these throw on the nature of the disease.

Still's disease is defined clinically as a form of chronic arthritis with swelling of the lymph glands and spleen. The swellings of the joints and lymph glands are usually multiple and symmetrical. The disease generally starts before the second dentition (Still, 1897; Simonetti, 1930) but sometimes occurs in adults (Strauss, 1926; Micheli and Gamna, 1928). The onset is usually insidious but sometimes acute and often accompanied by fever. The course is chronic; intermissions of fever may be associated with regression of the swellings of the joints, glands and spleen but both fever and the other changes often recur (Still, 1897; Simonetti, 1930; Bini, 1935). To the three cardinal signs may be added, in order of frequency: anaemia, muscular atrophy, cachexia, pericarditis, pleurisy, exophthalmos (Bini, 1935) and exanthemata (Simonetti, 1930).

Case report

S. W., a boy aged four years, was admitted to St. Mary's Hospital, Manchester, in April, 1943. The course of the disease was as follows: November, 1942, the knees were stiff and painful but the patient walked fairly well. April, 1943, there was a fusiform swelling of knees, elbows, metacarpophalangeal and interphalangeal joints of the hands; these were not tender nor were the joints fixed. Muscle wasting was severe and there was loss of weight. May, 1943, a bout of intermittent pyrexia lasting a fortnight, temperature ranging from 100° to 106° F. The joints were painful. Towards the end of the attack and following it for about a week there was a papular eruption all over the body.

June, 1943, there was a brief recrudescence of rash in another bout of pyrexia.

August, 1943, an enlarged gland was found in the right groin, and about a week later many small glands were palpable in neck and axillae.

September, 1943, the left hip was almost fixed and the right was adducted and flexed. Both knees were held in 60° flexion, reducible to 20°; there seemed to be an effusion. There was a valgus deformity of the right ankle and a flexion deformity and swelling of both wrists.

November, 1943, the spleen was felt for the first time about the middle of the month; bronchopneumonia occurred at the end of the month.

December 1, 1943, pericarditis was found.

December 7, 1943, the child died.

Laboratory findings. The following are representative blood counts:

12.4.43. Hb. 62 per cent. Red blood cells, 3·6 million. White blood cells, 6900/c.mm.

16.8.43. Hb. 72 per cent. Red blood cells, 4·5 million. White blood cells, 7200/c.mm.

8.10.43. Hb. 70 per cent. Red blood cells, 5·2 million. White blood cells, 6900/c.mm.

BACTERIOLOGICAL EXAMINATION of the faeces, nasopharynx and tonsils showed no significant abnormality.

VON PIRQUET'S TEST was negative.

RADIOLOGICAL EXAMINATION of the joints showed no significant change.

Summary of the relevant post-mortem findings. The lymph glands at the bifurcation of the trachea, along the splenic vessels and in the mesentery were enlarged (1·5 × 0·75 cm.), and those in the popliteal fossa were enlarged to a less extent. They were discrete, firm and elastic and had a uniform grey appearance on section. There was a fibrinous pericarditis with a few recent fibrous adhesions, a fibrinous pleurisy on the right side and bilateral bronchopneumonia. The liver (840 gm.) was moderately fatty. The spleen (160 gm.) was enlarged for the age and there was a fibrinous exudate on the surface.

The left knee was excised. Its capsule was thickened. The infra-patellar pad of fat and both surfaces of the semilunar cartilages were hyperaemic. A number of pits were present in the cartilage of the upper end of the tibia under the semilunar cartilages (fig. 1). On the femoral condyles were similar but shallower pits; these were pink.

The other organs showed no significant abnormality.

Histological findings. KNEE. The synovial membrane reflected on to the articular cartilage was infiltrated with lymphocytes and the lymph channels were dilated. The underlying cartilage was eroded. The cartilage in the centre of the joint surface had a fibrillar structure for a depth of ½–1 mm. The pits (fig. 2) were partly filled with a loose reticular tissue composed of argyrophilic fibrils, stellate cells and lymphocytes, which was covered by a layer of flattened cells. The fibrils ran in all directions but at the margins tended to lie at right angles to the surrounding cartilage (fig. 3). A few of them could

FIG. 1.—Part of the head of the left tibia showing the pits which underlay the semilunar cartilage (× 2).

FIG. 2.—Vertical section of a pit on the surface of the femoral condyle (H. and E. × 35).

FIG. 3.—The edge of a pit showing the argyrophil fibrils at right angles to the cartilage (silver impregnation × 300).

be traced into the hyaline cartilage. Many of the stellate cells contained fat globules, in this respect and in morphology closely resembling the cartilage cells (fig. 4). There were also spaces lined by swollen endothelium, some containing red cells whilst others, probably lymph vessels, were filled with fat. Cavities similar to these pits were present in the depth of the cartilage; these were filled with a similar reticular tissue which, however, contained no lymphocytes. Some of these cavities communicated with the ossification centre. One of the superficial pits (fig. 2) showed a detached island of cartilage.

On the surfaces of the infra-patellar pads of fat were scattered deposits of fibrin, some partially organized. The underlying tissue showed a widespread chronic inflammatory reaction. The infiltration was mostly lymphocytic but a few plasma cells and polymorphs were present and a moderate number of macrophages. In some places the leucocytes had a perivascular distribution.

SPLEEN. The pulp was packed with polymorphs as in the so-called septic spleen. The sinuses were conspicuous owing to swelling of the littoral cells. The argyrophilic reticulum was conspicuous but van Gieson's stain showed no increase in collagen. There was a hyaline thickening of the intima of most of the small arteries. The appearances were those of early 'fibro-adénie' as seen in splenic anaemia.

THE LYMPH GLANDS varied in appearance. (1) The abdominal glands were congested; the sinuses were dilated and loosely filled with lymphocytes and histiocytes, some of the littoral cells were swollen. The follicles were poorly defined and only a few

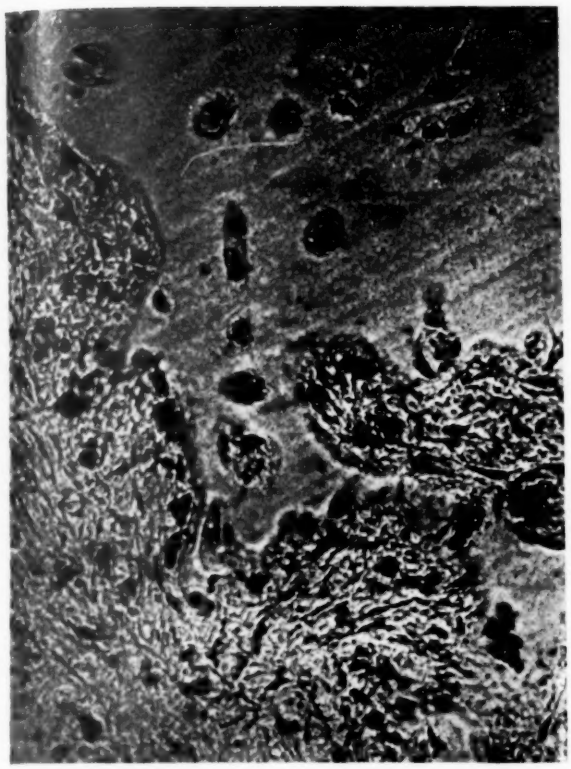

FIG. 4.—The edge of a cavity in the cartilage showing the fat droplets (black) in the cells of the cartilage and cavity (Sudan IV and Haemalum × 300).

had 'germinative' centres. In the medulla were a few groups of large cells with pale voluminous, oval or reniform nuclei with one or two nucleoli. Their cytoplasm stained faintly and was ill-defined with projecting fingers. These were either reticulum cells or undifferentiated mesenchymal cells. Mitoses were uncommon. These groups of cells were not present in all glands. Associated with them were histiocytes, some showing erythrophagocytosis. (2) The popliteal glands were similar to the abdominal ones except that there was much fibrosis extending from the hilum into the centre and some of the groups or voluminous cells appeared to surround vascular spaces and sinuses.

Microscopic examination of the pericardium, myocardium, lungs, liver, and kidneys confirmed the naked eye appearances. The bone marrow appeared normal. Nowhere were Aschoff nodules or tubercle bacilli found.

Discussion

Morbid anatomy. The anatomical changes reported by previous authors are summarized in the table.

THE JOINTS may show chronic inflammation of the soft tissues (Stoye, 1926; Levi, 1935) but Bini (1935) found no change. Only one previous case showed pits in the articular cartilage (Still, 1897) and no histological description was given. The pits in the present case were probably produced by a degeneration of the interstitial substance of the cartilage. This is suggested by the fragments of cartilage lying free in the reticular tissue of the pits (fig. 2) and confirmed by the similarity of the stellate cells to the cells of the surrounding cartilage and the arrangement of many of the argyrophil fibrils. These fibrils were at right angles to the margins of the cavity, as if they were a continuation of the argyrophil fibrils of the cartilage itself, described by Bloom (1943), and not a new formation. The free fat in the endothelial lined spaces is probably a product of degeneration.

LYMPH GLANDS have been examined more often than any other organs, since biopsy of these is easy. The descriptions vary. This may partly be due to the following factors, viz. (1) the changes in the glands are progressive (Simonetti, 1930); (2) the size of the glands, and hence probably the histological appearances, vary with the phase of the disease (Simonetti, 1930; Benedettelli, 1934); (3) although the enlargement of the glands is general, it is most marked near the affected joints (Still, 1897; Benedettelli, 1934). In the present case the changes in the popliteal glands were more advanced than in the abdominal ones. In Benedettelli's case the wrists were particularly affected and the changes in the epitrochlear glands more marked than in the axillary and inguinal glands. Sinus catarrh and the formation of germ follicles are the most usual changes (Micheli and Gamna, 1928; Simonetti, 1930; Benedettelli, 1934; Bini, 1935; Oggioni and Toldo, 1935; Levi, 1935 and 1938). Both changes are usually present in the same gland but sometimes they occur independently of one another. Such changes are commonly seen in lymph nodes draining sites of pyogenic infection but, according to Robb-Smith (1938), they are seldom found in generalized lymph node enlargement. Levi (1935, 1938) found ectopic haematopoiesis in both his cases. Maximow (1907) states that Dominici found ectopic haematopoiesis in glands in chronic infections and Lang (1935) gives a list of infections in which myeloid metaplasia has been found. The fibrosis found in the glands in cases of long duration (Oggioni and Toldo, 1935; Levi, 1938; and in the present case) suggest a chronic inflammatory reaction.

Thickening of the capsule of lymph glands has been reported by Strauss (1926), Oggioni and Toldo 1935) and Levi (1935); Levi's case also showed infiltration of the capsule with lymphocytes as did some of the glands in Bini's (1935) third case. Erythrophagocytosis was present in two of Bini's cases and in Levi's (1935) as in the present case. Plasma cells and eosinophilic leucocytes have been found in the cords and sinuses of the glands (Micheli and Gamna, 1928; Bini, 1935; Levi, 1935 and 1938).

The nature of the disease. The disease has been variously regarded as (1) a form of tuberculous rheumatism, (2) a type of rheumatic fever, (3) an endocrine disorder, (4) a form of rheumatoid arthritis, or (5) an independent disease. The evidence in favour of each view will be briefly discussed.

TUBERCULOSIS. Edsall (1904) injected old tuberculin in a boy of thirteen years suffering from

Still's disease and produced a general reaction and a local reaction in the affected joints; he found tubercle-like bacilli in the axillary glands but there was no histological evidence of tuberculosis nor did an emulsion of the glands produce tuberculosis in guinea-pigs. In Cozzolino's (1913) patient, who had previously suffered from tuberculous dactylitis, the tuberculin test caused a reaction in the affected joints. These observations have been thought to show that Still's disease is a form of toxic polyarthritis similar to the tuberculous rheumatism described by Poncet (1901). According to Brav and Hench (1934) the existence of tuberculous rheumatism is still undecided. Parkes Weber (1905) and Cunliffe (1907) regarded their cases as tuberculous because of positive tuberculin skin reactions. Most other authors report a negative tuberculin reaction (Koeppe, 1912; Longo, 1917; Simonetti, 1930; Benedettelli, 1934; Bini, 1935; Oggioni and Toldo, 1935). No tubercle bacilli have been found in sputum (Longo, 1917; Oggioni and Toldo, 1935), blood cultures (Oggioni and Toldo, 1935) or pleural fluid (Benedettelli, 1934) or in the glands (Micheli and Gamna, 1928; Simonetti, 1930; Benedettelli, 1934), whilst none of the authors cited in the table found evidence of tuberculosis at necropsy. This evidence confirms the present findings and does not support the tuberculous etiology of Still's disease despite the occasional suggestive clinical features (Koeppe, 1912; Longo, 1917). Reitano (quoted by Levi, 1935), however, takes the view that Still's disease may be due to various causes, tuberculosis being one.

RHEUMATIC FEVER. Longo (1917) suggested that Still's disease may be a form of rheumatic fever since cardiac complications and subcutaneous

TABLE SHOWING CHANGES FOUND AT NECROPSY (EXCLUDING LYMPH GLANDS)

Author	Joints	Spleen	Serous cavities	Heart
Still (1897)	Three cases examined. Capsule thickened. Hyperaemia of synovia. Fibrous adhesions. Cartilage pitted in one case.	Enlarged in each case.	Each case. 1. Adherent pericardium. 2. Pleural adhesions.	—
Koeppe (1912)	Capsule of knees slightly thickened.	Enlarged.	Adherent pericardium.	—
Iseke (1923)	—	Enlarged.	—	Tricuspid endocarditis.
Stoye (1926)	Knee: chronic inflammation of synovia and capsule.	1. Enlarged. 2. Perisplenitis.	Adherent pericardium.	Sclerosis of pulmonary valve.
Strauss (1926)	1. Capsule of knee and elbow: no inflammatory change. 2. Erosion of cartilage. 3. Granulations in left elbow.	1. Enlarged. 2. No fibrosis. 3. Perisplenic adhesions.	1. Pericardium thickened. 2. Pleural adhesions.	—
Micheli and Gamna (1928) Case 2	—	1. Enlarged. 2. Atrophy of follicles. 3. Pulp-congested. 4. Hyalinization of walls of arterioles. 5. Haemosiderosis.	1. Adherent pericardium. 2. Pleural adhesions. 3. Peritoneal adhesions.	—
Bini (1935) Case 1	—	Follicles enlarged.	Pericardial adhesions.	—
Bini (1935) Case 2	Histologically normal.	Fibro-adénie.	Pericarditis.	Myocarditis.
Bini (1935) Case 3	Histologically normal.	1. Amyloid in follicles. 2. Haemosiderosis.	Pericarditis.	Myocarditis.
Oggioni and Toldo (1935) Case 2	1. Breaking up and notching of outer layers of cartilage. 2. Deeper: fatty and mucoid degeneration with necrosis in places. 3. No inflammation.	1. Fibro-adénie. 2. Hyalinization of walls of arterioles.	—	—
Levi (1935)	Chronic inflammation of periarticular connective tissue.	Proliferation of endothelium of follicular arterioles.	1. Adherent pericardium. 2. Pleural adhesions.	—

nodules occur in both conditions. Whilst pericarditis is common in Still's disease, occurring in eleven of the cases listed in the table, endocarditis is less frequent, being reported at necropsy only by Iseke (1923) and Stoye (1926). There is no necropsy report of mitral or aortic endocarditis though Parkes Weber (1903, 1905) and Poynton (1907) each reported a case clinically with endocarditis, presumably of these valves. Bini (1935) found myocarditis in cases 2 and 3 but it did not appear to be rheumatic. Longo (1917) found subcutaneous nodules in his first case but it is possible that this should be classed as Jaccoud's arthritis rather than Still's.

There is no report of Aschoff's nodules being found in the heart or joints in Still's disease. Fahr (1921, 1930) maintains that these must be present to make a diagnosis of rheumatic granulomatosis, but Young and McMahon (1935) pointed out that these nodules are not permanent structures so that when healing occurs only non-specific scars may be found. Thus there is no definite evidence in favour of the rheumatic hypothesis.

ENDOCRINE DISORDER. Bini (1935) examined the endocrine glands of three cases of Still's disease at necropsy, but found no abnormality although the possibility of there being some endocrine disorder is suggested by the frequent occurrence of exophthalmos (Still, 1897; Reimold and Stoeber, 1925; Koeppe, 1912) and the increase in blood calcium in some forms of infantile arthritis (Grenet and Casalis, 1934).

RHEUMATOID ARTHRITIS. The morbid anatomy of the joints in Still's disease as at present known is not sufficiently defined to differentiate it from that of rheumatoid arthritis of adults (e.g. see description of Young and McMahon, 1935). Hence it might be supposed that the diseases are the same and that the adenopathy and splenomegaly are merely additional features peculiar to childhood and which occasionally occur in adults (Strauss, 1926). Still (1897), however, pointed out that even advanced cases showed no bony changes whereas these occur early in rheumatoid arthritis, and that there occurs in children a disease in every clinical respect like rheumatoid arthritis in adults. He concluded that the two conditions are distinct entities.

AN INDEPENDENT DISEASE. The widespread enlargement of the glands, the fibro-adénie of the spleen and the multiple arthritis indicate that Still's disease is a generalized disorder. The glandular changes are consistent with its being infective in nature, which is in keeping with the inflammatory and degenerative changes in the joints. However, there is no reason to suppose it is a form of tuberculosis or rheumatic fever. Although differentiation from rheumatoid arthritis is less certain it is probable that Still's disease is an independent entity of unknown but probably infective etiology. Micheli and Gamna (1928), Simonetti (1930) and Levi (1938) take a similar view.

Summary

1. A case of Still's disease is described.

2. The anatomical changes in the joints and glands are discussed.

3. A summary of the morbid anatomical changes described in the literature of Still's disease is presented.

4. The nature of the disease is discussed and it is concluded that it is not a form of tuberculosis, rheumatic fever or an endocrine disorder but an independent type of arthritis of infective origin.

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DECREASE OF SERUM CHOLESTEROL ESTER IN HAEMOLYTIC DISEASE OF THE NEWBORN

BY

ARNE ROTHE-MEYER, M.D.

Medical Officer, E.M.S.

and

EVELYN M. HICKMANS, M.Sc., Ph.D.

(From the Children's Hospital, Birmingham)

The conception of the pathological entity of the three manifestations of haemolytic disease of the newborn: hydrops foetalis, icterus gravis and congenital haemolytic anaemia has been confirmed by the discovery of the Rhesus factor. Moreover, this discovery has allowed us finally to abandon any sharp clinical distinction between the two latter forms of the disease. This is in accord with the fact that icterus may or may not be accompanied by anaemia, while anaemia may occur with or without previous jaundice. There are still, however, many unsolved problems, amongst which the question of liver damage is outstanding.

It has long been recognized that the jaundice occurring in haemolytic disease of the newborn cannot be explained as a pure haemolytic icterus. The severity of the jaundice, the positive Van den Bergh reaction and the pathological changes in the liver all point to a toxic injury of the liver. Furthermore, some cases are associated with 'kernikterus' or with late development of cirrhosis. Gilmour (1944) in his recent work on the morbid anatomy of 'erythroblastosis foetalis' has discussed the various hepatic changes, and presumed a toxic jaundice due to liver damage. The immunological reactions due to the Rhesus factor which take place in the infant or foetus (reviewed by Taylor and Race, 1944) may afford a partial explanation for the toxic effect upon the liver.

It is well known that the serum cholesterol and its partition may exhibit characteristic changes in diseases of the liver. Thannhauser and Schaber (1926) reported eleven cases of parenchymatous liver disease, in which they found decrease of the ester fraction of the serum cholesterol with absolute and relative increase of the free cholesterol, whereas the total cholesterol values were within normal limits. In acute yellow atrophy the ester fraction had disappeared completely, a phenomenon they termed 'Estersturz' (ester drop). These findings were confirmed by other investigators who have been quoted by Epstein and Greenspan (1936). These authors themselves evaluated the clinical significance of the cholesterol partition in hepatic diseases by investigation of a large number of cases. Obstructive jaundice is characterized by a hypercholesterolaemia, affecting both the free and the ester fraction, which parallels the degree of hyperbilirubinaemia. In acute parenchymatous degeneration, especially toxic and infectious hepatitis, on the other hand, the values for total cholesterol are normal or slightly sub-normal and show no relationship to the bilirubin values. The outstanding change here is the lowering of the ester fraction, which mirrors the severity of the liver damage. In the severest cases the ester fraction is low or absent, and remains so until the fatal end. In less severe cases the low values rise to normal with clinical improvement, while in mild cases there is only moderate depression of the ester values. More recently, Gray (1940) has confirmed these observations and has also found that a long-standing complete absence of the esterified cholesterol is a bad prognostic sign. He emphasizes that in acute parenchymatous liver disease the changes of the cholesterol ester fraction are more frequent and marked than are changes in the serum proteins.

As a part of investigations on liver function tests in infancy, determinations have been made of serum cholesterol and its partition in a group of infants suffering from haemolytic disease of the newborn. This paper records the results and attempts to assess their significance.

Information concerning the normal values for serum cholesterol during infancy is rather scarce. Sperry (1936), using the method of Schoenheimer and Sperry (1934), found values for total cholesterol ranging from 71 to 190 mgm. per cent. with an average of 133 mgm. per cent. in babies aged four to twenty-five days. At birth, figures were considerably lower, but there was a pronounced rise during the first three to four days of life, and the level during the period four to twenty-five days was fairly constant. He found that in this age group the ester fraction made up 41 to 72 per cent. of the total cholesterol, a variation range much bigger than had been found in children over two years of

age and in adults, who had an almost constant range of the ester fraction, limited to 70 to 75 per cent. of the total cholesterol. Physiological jaundice developed in about 30 per cent. of Sperry's group of sixty-three infants, but it neither affected the total cholesterol nor the cholesterol partition, an observation which forms a striking contrast to findings in haemolytic disease of the newborn.

No control figures are available for the method in the first three months of life, but unpublished results on eighty-two 'healthy' infants between three and twelve months of age, who came to the out-patient clinic for circumcision and minor surgical ailments, have shown values for total cholesterol between 98 and 230 mgm. per cent. while the variation range for the percentage of esterified cholesterol was 30 to 80. This is a slightly wider range than Sperry's for younger infants, and in the interpretation of our findings in haemolytic disease, therefore, we have only accepted cholesterol ester values of less than 30 per cent. of the total cholesterol as significantly abnormal.

The thymol turbidity test, recently described by Maclagan (1944), was also included in the investigation. It is considered by the author to be analogous to the colloidal gold reaction but to be a more sensitive liver function test. In normal adults values up to 4 units have been found and similar amounts have been measured in fifty 'healthy' infants between three months and twelve months of age.

Materials and methods

The subjects for investigation were fifteen in-patients at the Birmingham Children's Hospital. Blood for analysis was taken from a scalp vein three or four hours after the last meal. No attempt was made to obtain the samples under fasting conditions, as the cholesterol values may be regarded as fairly independent of alimentary fluctuations (Heymann and Rack, 1943).

Determination of cholesterol. EXTRACTION. Lipoids were extracted from the serum by slowly running 1 c.cm. into approximately 15 c.cm. alcohol-ether mixture (3 : 1) after the method of Bloor (1929). This mixture was heated with rotation in hot water, cooled and then filtered, the precipitate being washed with alcohol-ether and the filtrate made up to 25 c.cm.

TOTAL CHOLESTEROL. 2 c.cm. of the filtrate were measured directly into the macro-colorimeter tube of the Evelyn colorimeter (1936), evaporated to dryness and redissolved in approximately 5 c.cm. chloroform. The Liebermann colour reaction was developed by adding 2 c.cm. acetic anhydride and 0·2 c.cm. concentrated sulphuric acid, and the final volume made to 10 c.cm. with chloroform. The maximum reading on the colorimeter galvanometer was taken (usually about ten minutes after mixing), using filter 660, and values determined from a standard curve previously prepared from known amounts of cholesterol in the same way. The quantities here cited usually gave galvanometer readings between 50 and 70.

FREE CHOLESTEROL. The classical method of precipitation by digitonin followed by Bloor's method (1929) of oxidation with silver dichromate was used with some modifications here described in detail. 10 c.cm. of the alcohol-ether extract were evaporated to dryness in a graduated centrifuge tube and the residue re-extracted with petroleum ether. After centrifugation the petroleum ether fraction was transferred to another centrifuge tube and concentrated to about 1 c.cm. over a steam bath. The phospholipids were then precipitated with acetone and magnesium chloride in the usual way. The acetone supernatant liquid was transferred to another centrifuge tube and evaporated to approximately 6 c.cm. Then 1 c.cm. of a saturated solution of digitonin in alcohol was added and the mixture allowed to stand for an hour or so. After evaporation to dryness the residue was washed with ether without disturbing the solid. After removing the ether by centrifugation and decanting, 2 c.cm. water were added to the residue and allowed to stand for some time (preferably overnight) to ensure complete solution. Subsequently 6 to 7 c.cm. acetone were added and after stirring well it was centrifuged and decanted. The residue was washed successively with (1) acetone, (2) acetone +ether and (3) ether, stirring well each time. The final washed precipitate was dissolved in methanol, transferred to the oxidation flask, and after removing the methanol, the residue was treated with silver dichromate as described by Bloor (1928).

Determination of serum proteins. A micro method, involving nitrogen determination by Kjeldahl digestion and photometric estimation after Nesslerization was used.

Determination of bilirubin. At the beginning of the investigation Van den Bergh's method giving results in units was used, but later, a quantitative micro-method, combining details from Malloy and Evelyn (1937) and from Haslewood and King's (1937) methods giving results in mgm. per cent. was substituted. As the values for serum proteins and bilirubin are only given for the sake of completing the clinical notes, the methods employed are not described in detail.

The thymol turbidity test. Maclagan's method was used without modification.

Results

Among the fifteen patients listed in the table, cases 3, 5 and 11 are examples of icterus gravis without anaemia, while cases 8, 13 and 15 represent anaemias without jaundice. The others enter an intermediate classification suffering from both icterus and anaemia. The Rh factor in mother and child was of the typical combination except in case 5 which represents a rare Rh intergroup immunisation. Anti-Rh agglutinins were found in all mothers with the exception of case 4. (The Rh investigations were done by Dr. H. S. Baar, pathologist to the Children's Hospital.)

The jaundice, when present, was of varying degree and duration, but was usually of sufficient severity to imply a diagnosis of haemolytic disease of the newborn on admission. The cases of anaemia showed the typical haemolytic picture with pronounced reduction of haemoglobin and red cell counts frequently associated with 'peripheral erythroblastosis.' The only exception is case 15, which at the time of the first examination presented a hypoplastic anaemia, and in spite of repeated transfusions this persisted during the first seven months of the patient's life. As the first cholesterol

TABLE 1

SUMMARY OF FIFTEEN CASES INVESTIGATED

Clinical data	Age in days	Cholesterol: mgm. per cent.			Protein: gm. per cent.			Thymol Test	Bilirubin:	
		Total	Ester	Free	Total	Alb.	Glob.		Direct	Total
1. BERT M. born 7.3.35. B.W. ? child No. 4	1	91	10	81						
FAMILY HISTORY: no previous icterus (1943: child O Rh+; mother A Rh− (+anti-Rh aggl.))	5								+	3 units
JAUNDICE: 1st day, fading from 8th day	6								+	9 units
ANAEMIA: no blood counts available; present on 12th day	8								+	6·5 units
TRANSFUSION: 12th day	11								+	2 units
2. MICHAEL R. born 13.8.43. B.W. 7 lb. 2 oz., child No. 2										
FAMILY HISTORY: no previous jaundice	5	176	14	162					+	12·8 units
RH.: child O Rh+; mother A Rh− (+anti-Rh).										
JAUNDICE: 2nd day, fading within 4 weeks	21								+	5·5 units
ANAEMIA: between 3rd and 5th day. Hb. 61 per cent.; red blood cells 2·52 million.										
TRANSFUSION: on 7th and 8th day.										
3. BABY (♂) W. born 4.1.45. B.W. 6¾ lb. child No. 3	2	101	0	101	3·97	2·60	1·37		−	6·7 units
FAMILY HISTORY: No 2 survived icterus gravis.										
RH.: child A Rh+, mother A Rh− (+anti-Rh).										
JAUNDICE: 1st day, fading within 12 days.										
NO ANAEMIA: for 25 days, then infection—anaemia, recurrent jaundice. Anaemia improves after.										
TRANSFUSION: 30th day, but septic condition aggravates.										
DIED 35th day. AUTOPSY: icterus gravis, incipient hepatic cirrhosis, colitis with intestinal pneumatosis, purulent otitis media.										
4. ANTHONY C. born 21.1.45, B.W. 7¼ lb. child No. 2.										
FAMILY HISTORY: No. 1 died from icterus gravis	12	126	0	126	5·62	2·64	2·98	<1	+	per cent. 12 mgm.
RH.: child A Rh+, mother O Rh−, father A Rh+.										
JAUNDICE: 2nd day, fading within 3 weeks	40	120	88	32	4·43	3·39	1·04	2·5	−	0·1 mgm.
ANAEMIA: on 2nd day, Hb. 50 per cent., red blood cells 2·20 million.										
TRANSFUSION: 2nd and 12th day.										
5. KENNETH S. born 18.1.45, B.W. 7½ lb., child No. 2.										
FAMILY HISTORY: no previous icterus	29	123	0	123	4·59	2·99	1·60	1	+	11 mgm.
RH: Child O Rh, rh (+Race Wiener anti-body), father O Rh, rh, mother O Rh, rh (+anti-Rh aggl.).										
JAUNDICE: at birth, increasing several days, lasted over 4 weeks	49	98	22	76				1	−	0 mgm.
NO ANAEMIA—NO TRANSFUSION. KERNIKTERUS developed.										
6. RAYMOND H. born 10.2.45, B.W. 6½ lb. Twin, No. 3 or 4	5	151	6	145	5·32	3·01	2·31	0	+	45 mgm.
FAMILY HISTORY: no previous icterus.										

TABLE I—*continued*

Clinical data	Age in days	Cholesterol: mgm. per cent.			Protein: gm. per cent.			Thymol Test	Bilirubin:	
		Total	Ester	Free	Total	Alb.	Glob.		Direct	Total
RH: child O Rh+, mother A Rh− (+ anti-Rh)	26	157	66	91	5·10	2·92	2·18	1·5	+	per cent. 18 mgm.
JAUNDICE: 2nd day, fading after 6 weeks. ANAEMIA: within 18 days, Hb. 61 per cent., red blood cells 3·50 million .. TRANSFUSION: 18th and 55th day.	44	165	80	77	3·85	2·26	1·59	1·0	+	6 mgm.
7. JOHN H. born 10.2.45, B.W. 6 lb. Twin, No. 3 or 4 .. .. .. FAMILY HISTORY and RH FACTOR as in case 6.	5	156	31	125	4·81	2·86	1·95	<1	+	28 mgm.
JAUNDICE: 2nd day, fading within 3 weeks	26	97	47	50	4·50	2·84	1·66	<1	+	5·8 mgm.
ANAEMIA: 4th day, Hb. 70 per cent., red blood cells, 3·28 million .. TRANSFUSION: 4th, 23rd, and 55th day	44	110	38	72	4·50	2·84	1·66	2	−	0·9 mgm.
8. DAVID C. born 24.12.44, B.W. 7 lb. Child No. 3. FAMILY HISTORY: no previous icterus. RH: child A Rh+, mother O Rh− (+anti-Rh)	38	141	39	102	4·07	1·94	2·13	1	−	1·3 mgm.
NO CLINICAL JAUNDICE. ANAEMIA: 38th day, Hb. 28 per cent., red blood cells 1·38 million .. .. TRANSFUSION: 38th day.	54	139	36	103	4·44	3·19	1·25	1	−	0·65 mgm.
9. RONALD E. born 19.1.45. B.W. 5 lb., child No. 3 .. .. FAMILY HISTORY: No. 2 died from jaundice at 2 days old. RH: child O Rh+, mother O Rh− (+anti-Rh). JAUNDICE: 1st day, fading after 1 week. ANAEMIA: 4th day, Hb. 55 per cent., red blood cells 2·37 million. TRANSFUSION: 6th and 15th day.	5	148	45	103	4·75		1·0	1	+	20 mgm.
10. CAROLE D. born 6.3.45, B.W. 7 lb., child No. 2. FAMILY HISTORY: no previous icterus RH: child A Rh+, mother A Rh− (+anti-Rh). JAUNDICE: at birth, fading within 2 weeks. ANAEMIA: 16th day, Hb. 48 per cent., red blood cells 1·97 million. TRANSFUSION: 16th day.	16	86	39	47	5·31	3·50	1·81	1	−	2·4 mgm.
11. JOHN O'K. born 4.12.44, B.W. 6¾ lb., child No. 2. FAMILY HISTORY: no previous icterus RH: child O Rh+, mother O Rh− (+anti-Rh). JAUNDICE: 3rd day, fading within 3 weeks. NO ANAEMIA—NO TRANSFUSION.	14	166	87	79	5·18	3·69	1·49		−	2 units
12. MICHAEL H. born 15.11.44, B.W. 5¾ lb., child No. 3. FAMILY HISTORY: no previous icterus RH: child O Rh+, mother A Rh− (+anti-Rh). JAUNDICE: 1st day, fading within 2 weeks. ANAEMIA: between 5th and 12th day, Hb. 60 per cent., red blood cells 2·23 million. TRANSFUSION: 16th and 44th day.	7	103	55	48	4·70	2·41	2·29			

TABLE I—*continued*

Clinical data	Age in days	Cholesterol: mgm. per cent.			Protein: gm. per cent.			Thymol test	Bilirubin:	
		Total	Ester	Free	Total	Alb.	Glob.		Direct	Total
13. BABY (♂) B. born 21.2.45, B.W. ? child No. 3. FAMILY HISTORY: No. 2 died from icterus gravis RH: child A Rh+, mother A Rh− (+anti-Rh). NO CLINICAL JAUNDICE. ANAEMIA: 7th day, Hb. 29 per cent., red blood cells 0·94 million. TRANSFUSION: 7th and 14th day.	7	175	123	52	6·25	3·78	2·47	<5	+	per cent. 2·7 mgm.
14. BABY (♂) W. born 15.6.43, B.W. 7 lb., child No. 3. FAMILY HISTORY: no previous icterus RH: child O Rh+, mother O Rh− (+anti-Rh). JAUNDICE: 1st day, fading within 3 weeks. ANAEMIA: 3rd day, Hb. 70 per cent., red blood cells 2·72 million. TRANSFUSION: 10th and 15th day KERNIKTERUS developed.	4	132	100	32					+	20 units
15. DEREK C. born 13.7.44, B.W. ? child No. 8. FAMILY HISTORY: 1 child died from anaemia in infancy. RH: child A Rh+, mother A Rh− (+anti-Rh). NO JAUNDICE OBSERVED ANAEMIA: 66th day, Hb. 32 per cent., red blood cells 1·83 million. Hypoplastic anaemia persisted until age of 8 months. TRANSFUSION: 8 transfusions between 67th and 200th day of life	101 215	113 142	87 90	26 52	 4·81	 3·58	 1·23	 2	 —	 per cent. 0·3 mgm.

estimation was only made when the child was a hundred days old, i.e. at the time when a cholesterol ester decrease might have been compensated, this case will be excluded from the following discussion.

The remaining fourteen cases show values for total cholesterol within normal limits. Nine of these fourteen cases however, showed a marked decrease of the esterified cholesterol fraction, which in six cases (no. 1 to 6) represents 0 or less than 10 per cent. of the total cholesterol, while three cases (no. 7 to 9) render values between 20 per cent. and 30 per cent. of the total cholesterol.

The cholesterol ester decrease may be present on the first day of life (case 1) and has, in untreated cases, been found present as late as the twenty-ninth and thirty-ninth day (cases 15 and 8). The duration of the 'ester drop' has not yet been defined. Repeated estimations were done in five cases; the ester fraction had regained normal values on the twenty-sixth, twenty-sixth and fortieth day in cases 4, 5 and 6, while two cases still showed a marked ester decrease on the forty-ninth and fifty-fourth day (cases 5 and 8).

Blood transfusion does not appear to accelerate the restitution of the esterified cholesterol. Case 4 showed extreme ester decrease on the twelfth day of life in spite of previous transfusion, and in case 8 the low ester value remained unchanged from the thirty-ninth to the fifty-fourth day despite transfusion between these dates.

TABLE 2

DISTRIBUTION OF CASES IN REGARD TO JAUNDICE AND ANAEMIA

	+Cholesterol change	−Cholesterol change	Total
JAUNDICE WITHOUT ANAEMIA	2	1	3
JAUNDICE PLUS ANAEMIA	6	3	9
ANAEMIA WITHOUT JAUNDICE	1	1 (+1)	2
TOTALS	9	5	14

No appreciable correlation between the cholesterol ester decrease and the onset, degree and duration of the jaundice or of the anaemia could be demonstrated in this investigation. It is interesting to notice that the marked 'ester drop' occurs in one case (no. 8) in which a clinical jaundice had never been observed, and in two cases (no. 3 and 5) which did not develop any anaemia. Of the two cases

associated with kernikterus, one presented the ' ester drop ' (case 5), the other did not (case 14).

The thymol turbidity test was performed in six of the nine cases with cholesterol ester changes, and in two of the five cases without such changes; it showed normal values in all these cases, the figure of 5 units in case 13 not being significant as it occurred in lipaemic serum.

Conclusions

The changes in the cholesterol partition which have been found in nine out of fourteen cases of haemolytic disease of the newborn are quite similar to those demonstrated as characteristic of acute toxic injury of the liver. No explanation can be offered for the fact that in five cases in the series no such changes were found. Admittedly these cases may have been less severe, but there does not seem to have been any essential deviation in clinical type or course to account for the difference. In this connexion it will be well to remember two points. Firstly, the typical changes reported in the literature have not been found in all cases where from the clinical aspect they might have been expected. Secondly, it is still unknown which function or dysfunction of the liver is involved when there are changes of the serum cholesterol partition.

Many questions have been left unanswered in the investigation, because the series was too small. The frequency and the duration of the cholesterol changes and also the relationship of these changes to jaundice (and possibly anaemia) have still to be settled. More information is needed concerning the morbid anatomy of the hepatic changes during the acute stages of the haemolytic disease. This may be obtained, if a procedure of intervital liver biopsy which is safe for infants can be evolved. Finally, the possibility of a correlation between the cholesterol changes and the agglutinin titre in the blood of the mothers and infants has to be investigated. It is hoped that this report will induce investigators who have the opportunity, to take up some of these problems.

Summary

The serum cholesterol partition in fourteen cases of haemolytic disease of the newborn was determined.

The values for total cholesterol were within normal limits in all cases.

Nine of the fourteen cases showed a marked decrease or complete absence of the esterified fraction of cholesterol, findings quite similar to those demonstrated as characteristic of acute toxic liver injury.

The thymol turbidity test of Maclagan, which was performed in six of the nine cases, showed normal values.

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OSTEOMYELITIS OF THE JAWS IN INFANCY

TREATED WITH PENICILLIN

BY

N. M. JACOBY, M.D., M.R.C.P.

Registrar to the Children's Department, Guy's Hospital; Physician E.M.S.

and

L. SAGORIN, M.R.C.S., L.R.C.P., D.C.H.

Paediatric R.M.O., Pembury Hospital, E.M.S.

Osteomyelitis of the maxilla is a rare condition, about eighty cases having been reported since 1847. It produces a characteristic clinical picture, making recognition easy. Asherson (1939) in England and Lacy and Engel (1939) in the U.S.A. have given detailed accounts of the clinical picture and the differential diagnosis and have discussed the etiology and reviewed the literature. Their views on the treatment and prognosis agree fairly closely, but as these views antedate the use of penicillin, they are no longer tenable.

The condition is practically confined to infants under the age of twelve weeks, whose previous history in relation to delivery and feeding is not significant. The condition has generally been progressing for several days before it is recognized as being one of more than mere local inflammation. In the present cases, this period averaged eight days. The characteristic feature is gross swelling of the affected side. In the case of the maxilla both eyelids are involved with proptosis and chemosis; the cheek is remarkably swollen and indurated. In addition there is frequently a unilateral purulent nasal discharge and occasionally pus discharges externally from below the inner canthus of the eye. Inside the mouth the alveolus and the hard palate are swollen and inflamed, and sinuses may be discharging either from the alveolus or the bucco-gingival fold; the bucco-gingival space may be markedly narrowed. When the mandible is involved the swelling is mainly in the submental region, whilst inside the mouth, although the lower jaw is affected, the condition is essentially the same. From any of the purulent discharges, staphylococcus aureus can be cultured.

The etiology of this condition is not completely explained, since the portal of entry of the staphylococcus is unknown. Asherson (1939), Lacy and Engel (1939) and Mowlem (1944) agree that the bone infection is of haematogenous origin, though there is no record of a positive blood culture in their cases. Unfortunately in the first two cases here described this investigation was also omitted, but in the one case in which it was done a heavy growth of staphylococcus aureus was obtained within twenty-four hours. In the case of the maxilla, the bone infection is, on anatomical grounds, presumed to start in the tooth socket of the first molar. In mandibular infections the theories that have been advanced are 'diminution of local immunity' and 'specific organismal infection,' but as Mowlem points out these theories are 'meaningless and incapable of proof.' Although the tooth buds are not in close proximity to the vessels it is possible that the infection settles in a tooth socket.

Case reports

Case 1. E. M. C., a male, aged twenty-four days. The infant was full term, and born by normal delivery, weighing 10 lb. 4 oz. at birth. He was breast fed, and was admitted on 9.8.44. At the age of fourteen days the mother noted swelling of the right upper gum, and the following day considerable swelling of the right face. At sixteen days pus was discharging from three sinuses in the gum.

On admission the infant was extremely ill, with temperature 102° F., pulse 130, and respiration 30 per minute. The right face was extremely swollen, and was indurated and red. Both eyelids were swollen, occluding the palpebral fissure; there was a discharge due to purulent conjunctivitis. The right side of the hard palate and upper alveolus were swollen and indurated. Pus was discharging from three sinuses on the alveolar margin.

TREATMENT. 9.8.44. OPERATION. Under general anaesthesia the right maxilla was opened through an incision of the gum. The sinuses were connected and about two drachms of pus was evacuated together with two small sequestra and four deciduous tooth buds. The resulting cavity was packed with vaseline gauze which was removed next day. (Culture from the pus gave a mixed growth of staphylococcus aureus and a few colonies of streptococcus haemolyticus. Both organisms were penicillin-sensitive.)

Post-operatively, intra-muscular penicillin 5000 units, was injected four-hourly.

11.8.44. Intramuscular penicillin 2500 units four-hourly, was given until 18.8.44, the total dose being 160,000 units in nine days.

The temperature subsided to 98·4° F. in twenty-four hours and did not rise again; the infant was obviously out of danger from this time on. The facial swelling did not subside appreciably and by 14.8.44 there were fluctuant swellings over the right maxilla and below the inner canthus of the right eye.

15.8.44. 1 oz. pus was aspirated from within the mouth to drain the maxillary swelling. Pus below the inner canthus was aspirated from the skin surface.

20.8.44. The face was now completely symmetrical, and all swelling had subsided.

24.8.44. Discharged from hospital. The infant was last seen in May 1945 and has remained well.

Case 2. A.J.B., male, aged ten weeks. The infant was born at full term by normal delivery, weighing 7 lb. 13 oz. and was breast fed.

1.1.45. The mother noticed a small boil below the chin.

10.1.45. Submental swelling was present over the whole of the left side of the lower jaw.

14.1.45. Pus was discharging into the mouth.

15.1.45. Patient was admitted to hospital. The infant was not acutely ill, the temperature being 100° F., the pulse 140, and the respiration 44 per minute. There was a large, red, indurated swelling under the left inferior margin of the mandible. The left lower alveolus and floor of mouth were swollen. Three sinuses were discharging from the alveolus. X-ray showed irregularity of the lower mandibular border.

TREATMENT. 15.1.45. Intramuscular penicillin, 7000 units four-hourly, was given until 22.1.45, the total dose being 280,000 units.

The temperature fell within twenty-four hours and within seven days all swelling and discharge had ceased.

30.1.45. Prophylactically, a second course of penicillin was given (175,000 units in three days).

6.2.45. Patient was discharged fit from hospital.

July 1945. The private doctor reports that the child has remained well.

Case 3. B. W., a male, aged six weeks, had been born two weeks prematurely of a diabetic mother after surgical induction. The delivery was normal, and the birth weight 8 lb. 9 oz. The infant was artificially fed on a full cream feed.

26.6.45. The mother noted that the left eye was puffy and the left side of the face swollen. There was a watery discharge from the eye, and some difficulty in breathing.

27.6.45. The swelling had increased, and there was a purulent (later blood-stained) discharge from the left nostril.

28.6.45. The patient was admitted to hospital. The infant was not acutely ill, the temperature being 103° F., the pulse 140, and the respiration 40 per minute. The left side of the face and the eye-lids were oedematous. There was a large, red, indurated, tender area over the left maxilla and a purulent discharge from the left nostril and eye. The nasal discharge increased on pressure over the maxilla. The left alveolus and hard palate were swollen and buccogingival space was narrowed but there was no sinus apparent.

Blood culture gave a growth of staphylococcus aureus, and a culture of the nasal discharge grew a similar organism which was penicillin-sensitive.

TREATMENT. 28.6.45. Intramuscular penicillin, 5000 units four-hourly, was given until 6.7.45, the total dose being 235,000 units.

29.6.45. A small sinus discharged in the posterior part of the left upper alveolus; a probe was inserted about $\frac{1}{8}$ inch.

The temperature fell to 98·4° F. in twenty-four hours and did not rise again. The swelling was subsiding by 30.6.45 and both this and the nasal discharge had completely disappeared by 6.7.45, when the sinus too was closed.

11.7.45. The patient was discharged from hospital. The infant was last seen on 1.8.45 and had remained well.

Comment

TREATMENT. In case 1 no previous experience of the use of penicillin in this condition was available. In retrospect it now appears that the surgery undertaken was far too radical and without such interference there would probably have been a smaller loss of deciduous teeth. Subsequent experience has taught us that the best procedure is to rely mainly on penicillin and to carry out only such surgical measures as may be necessary to remove obvious collections of pus. Thus whilst in case 1 an operation was performed first and penicillin used afterwards, in the subsequent cases penicillin was used from the very beginning and it was found that no surgery was required.

In case 2 where the mandible was involved, a second prophylactic course of penicillin was given one week after the termination of the first, as in view of the recurrences reported in other cases of osteomyelitis it was thought that a second course might help to prevent such a recurrence here. In the maxillary cases, response to initial treatment was excellent and considering the vascular nature of this bone in infancy, we did not think it necessary to repeat the penicillin.

PROGNOSIS. Penicillin therapy which has revolutionized the prognosis in so many infections, has apparently an equally dramatic effect in osteomyelitis of the jaws in infancy. Moreover, when dealing with infections of the face, not only must the threat to life be considered, but in those who survive the cosmetic result is of paramount importance.

In the past when treatment has consisted of free surgical drainage and more recently with the addition of sulphonamides, the mortality in 43 cases reported or collected by Marx (1922), Turner (1942), Magnus (1944), Asherson (1939) and Lacy and Engel (1939) was 31 per cent. In our three cases there were no deaths and though this series is too small to draw any definite conclusions, the fact that within twenty-four hours of starting treatment it was obvious that all the cases were going to recover and all danger had passed, leads us to deduce that in the future the mortality rate will be of a very low order.

The cosmetic result, judging from photographs of published cases treated by surgical drainage, has not

been perfect. There are usually one or more scars below the lower eye-lid and these scars appear to be fixed to bone with resulting 'pitting' of the area. In our first case in which pus was aspirated through the skin, scarring was minimal and there was no disfigurement. The subsequent cases had no scarring and the cosmetic result was perfect.

The loss of tooth buds is a further factor that should be mentioned, as it may lead to deformity and disfigurement when the teeth erupt later on. Rix, in a private communication, informs us that loss of tooth buds in the upper jaw is not likely to result in deformity, but when tooth buds are lost from the lower jaw the loss is more serious, as the shape of the upper dental arch appears to be controlled by the shape of the lower arch. As the loss of tooth buds is in part due to surgical intervention it is obvious that when penicillin is used and surgery is minimal, deformity due to loss of teeth of the primary dentition will also be minimal.

A last point worthy of mention is the remarkable rapidity with which penicillin cures the disease. Thus, whereas the average duration of the surgically treated cases is about three and a half months, and even after this period some of them still had discharging sinuses, our three penicillin-treated cases were completely cured and all sinuses healed in twelve days.

Summary

(1) The penicillin treatment of two cases of osteomyelitis of the maxilla and one of the mandible, in infancy, is described.

(2) The prognosis and cosmetic result are dramatically improved and the duration of the disease greatly reduced.

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THE MEASUREMENT OF THE NUTRITIONAL LEVEL OF THIAMIN IN CHILDREN BY THE ESTIMATION OF THE URINARY EXCRETION

BY

E. C. ALLIBONE, M.D. and E. FINCH, M.Sc.

(From the Children's Hospital, Birmingham)

The incidence of deficiency syndromes due to lack of the vitamin B complex is low in children living in temperate climates. Nevertheless, doubts have been raised as to whether a dietary intake, sufficient to prevent a frank deficiency state, was optimal for development.

Morgan and Barry (1930) found an increased weight gain on supplementing children's diets with wheat germ. Bloxsom (1929), using yeast, and Dennett (1929), using wheat germ sugar, recorded the same result with infants. Litchfield et al. (1939) found that the weight gain of prematures was accelerated by yeast. Poole et al. (1937) using rice polishings could not detect any acceleration in weight gain although the gain was steadier.

Justin and Helms (1937) supplemented the diet of fifty infants with vitamin B. Over a period of a year there was an increase of height and to a less extent of weight as compared with a similar number of controls. Elias and Turner (1936), using wheat germ and yeast, observed no difference in either height or weight gain, but anorexia was less frequent than in controls. They were of the opinion that added vitamin was unnecessary on a good diet.

From the above reports it may be assumed that, whereas a good diet may contain optimal amounts of vitamin B, this desideratum is often not attained.

Further attempts to determine the nutritional state of the individual with regard to thiamin were made possible when Harris and Leong (1936), by means of the bradycardia method, found the urinary output of thiamin to be dependent on the intake. The publication of the thiochrome method of estimation of thiamin in body fluids and tissues facilitated further study on the relationship between intake and output. Bicknell and Prescott (1942) tabulated the daily urinary excretion of normal adults. The results of nine groups of workers using the thiochrome method, ranged between 50 and 500 microgm. per day.

Benson et al. (1942) found in healthy children a daily excretion of at least 20 per cent. of the intake, the lowest figures being 100 microgm., the average being 270 microgm. per day. These workers considered the estimation of the daily excretion to be preferable to giving a loading dose of pure vitamin as large doses were insensitive and small doses gave too variable results. The daily output of urinary thiamin should be at least 20 per cent. of that ingested. Westenbrink and Goudsmit (1937), however, showed that in normal subjects on a thiamin poor diet for two to three days, the twenty-four-hour secretion fell to 40 microgm., suggesting that the estimation of the dietary excretion without administration of a test dose would in many cases only indicate the adequacy of the diet during the preceding few days. Wang and Yudkin (1940) also showed that the resting level did not give an accurate assessment of the state of nutrition and stipulated test doses for the detection of the presence and degree of deficiency.

For these reasons, coupled with the considerable variation in the excretion of the vitamin in normal subjects, many workers considered the degree of excretion after an oral test dose of 1 to 5 mgm. to be the more reliable guide. If large doses were given orally there was a failure of absorption. Ritsert (1938a), after an oral dose of 10 mgm. in an adult, found only 4 to 7 per cent. in the urine, there being 7 to 30 per cent. in the faeces. Karrer (1937) also found that the larger the oral dose the smaller the percentage excretion in the urine. A loading dose must therefore bear a close relationship to the needs of the organism.

The daily requirements of children had been variously estimated. Morgan and Haynes (1939) found that a well-fed woman excreted milk containing 32 microgm. of vitamin B_1 per 100 c.cm. Attempts to raise this figure by thiamin supplements to the maternal diet caused a fall in the excretion level to 25 microgm. per 100 c.cm. These findings agree with those of Knott, Kleiger and Schlutz (1943) who, from the results of thiamin excretion, considered that infants needed 40 microgm. per kgm. body weight. In older children Knott (1936) found a higher retention accompanying higher levels of intake, 60 microgm. per kgm. per day being the optimum amount. From these figures it would appear that an oral dose of 0·5 mgm. to infants and 1·0 mgm. to older children would be within physiological limits. The dose is usually given with a meal as Melnick and Field (1939) found that, when thiamin was given on a fasting stomach, less vitamin was excreted, suggesting that some was destroyed

in it, although a major excretion in the first four hours rather than in the first eight indicated that the thiamin was absorbed more rapidly on an empty stomach.

Hills (1939), who administered a test dose of 1 mgm. orally to adults, examined the excretion of vitamin during the next three hours, finding the maximum response during the second hour. Jowett (1940), using a 5 mgm. test dose considered the shortest period for collecting urine to be five hours, in which time a constant proportion (68 per cent.) of the twenty-four hour excretion was eliminated in normals although in patients there were greater variations. Borson (1940), who gave 0·1 mgm. per kgm. body weight considered that a normal person excreted 8 to 10 per cent. of the dose within five hours. Ritsert (1938b), however, used twenty-four-hour specimens, as did Melnick et al. (1939), having found delayed absorption of vitamin when given with a meal.

Present investigation

Type of case investigated. The children, who were in-patients, were drawn mainly from working-class homes. As the hospital was in a danger area from the point of view of air raids, the earlier cases had to be evacuated as soon as they were fit to travel. The subjects to be tested had to be well enough to be on an ordinary diet, to be reliable in their habits and not to be receiving either salicylates or chemotherapy. This restricted the choice of case. In the majority the test was limited to the collecting of urine on two consecutive days. The following day an oral dose of vitamin B_1 was given. Anomalous results unfortunately could not be checked as the cases had by this time either been discharged or evacuated.

In view of the frequent irregularity in absorption and excretion of urine in children, all urine, whether following a test or not, was initially collected in three periods from 6 a.m. to noon, noon to 6 p.m. and from 6 p.m. to 6 a.m.

Method. The urinary thiochrome was estimated after the method of Janson (1936). Wang and Harris (1939) have examined many possible sources of error and some of their modifications were used. The interference caused by non-specific fluorescent substances present in children's urine was very pronounced in many specimens. Their suggestion for a preliminary washing with iso-butyl alcohol certainly reduced this interference in many cases but in others there was left a fluorescence which produced such a high blank that the estimation had to be abandoned. It was found later that some of this fluorescence was due to the use of corks in the extraction tubes. The use of glass-stoppered flasks reduced this trouble considerably. A photo-electric fluorimeter was used for the measurement of the fluorescence. The tubes used to hold the fluorescent liquid were selected to give the minimum fluorescence in ultra-violet light when empty and all had practically the same small value in this respect. They were 1·9 cm. in diameter, this larger size having been found necessary to produce a reasonable deflection with urine specimens frequently low in thiamin. Iso-butyl alcohol was used for the final clearance of the solutions. The use of filter paper was avoided by centrifuging whenever necessary. No sodium sulphate was used.

Specimens were collected in stoppered bottles containing 10 c.cm. of glacial acetic acid for twenty-four hours and proportional amounts for shorter periods. If cloudy or showing a precipitate, a portion was centrifuged and the clear upper layer used for the estimation. If very concentrated and dark, it was mixed with an equal volume of water. A known aliquot, usually 10 c.cm., was shaken thoroughly with an equal volume of iso-butyl alcohol for at least a minute. After centrifuging, the volume of the aqueous layer was noted and then carefully removed. Three lots of 2·5 c.cm. of the urine were then transferred to three large test-tubes of 50 c.cm. capacity and 7·5 c.cm. of distilled water were added to each. To tubes 1 and 2, 3 c.cm. of 14 per cent. caustic soda were added and to tube 2 a solution of 1 per cent. potassium ferricyanide was immediately added with shaking and drop by drop until there was just an excess as indicated by a slight increase in the yellow colour. To tube 3 was added 0·2 c.cm. of a solution of thiamin containing 1 mgm. per 100 c.cm., followed by caustic soda and ferricyanide as in tube 2. After two minutes' standing, 12·5 c.cm. of iso-butyl alcohol were added to each tube and it was stoppered and shaken fairly gently for two minutes, afterwards standing till clear. 10 c.cm. of the iso-butyl alcohol layer were pipetted off from each tube and transferred to the fluorimeter tube. 1 c.cm. of dry ethyl alcohol was added to each tube to clarify. The readings were then made in the fluorimeter and the thiamin calculated. Tube 3 was used to determine the recovery value after addition of a standard quantity of thiamin. This usually ranged from 90 to 100 per cent. with an average of 94 to 95 per cent. The standard was prepared as follows. A solution containing 100 mgm. of thiamin in 100 c.cm. of water containing 2 drops of concentrated hydrochloric acid was prepared and diluted ten times. 1 c.cm. contained 100 microgm. To 1 c.cm. of this solution 3 c.cm. of 10 per cent. sodium hydroxide were added and 2 drops of 1 per cent. potassium ferricyanide. After standing for two minutes it was extracted with 20 c.cm. iso-butyl alcohol to give suitable dilutions in a volume of 9 c.cm. and 1 c.cm. of ethyl alcohol was added to clear. These tubes were read in the fluorimeter and a curve plotted of the galvanometer readings against the concentration of thiamin.

Since at low dilutions and with the apparatus in use the deflection is proportionate to the concentration, we have in the following work used only those concentrations within this range of dilutions, viz., between 0·1 and 0·4 microgm. per c.cm. Hills (1939) found that 'provided the thiamin content was not great, it was linearly related to the fluorescence of the oxidised extracts.'

Results. The twenty-four-hour urinary excretion showed a range of 10 to 400 microgm. Lower values were obtained in the younger age groups who had a lower calorie and vitamin intake. When the age groups were rendered comparable by expressing the excretion as a percentage of the intake the differences became less, ranging from an average of 10 per cent. in the youngest age group to 14 per cent. in the oldest (table 1).

ORAL LOADING TEST. Sixty-seven children were given an oral dose of 0·5 to 1·0 mgm. thiamin. The amount of this excreted in the following twenty-four hours varied from 0 to 41 per cent., with an average of 14·1 per cent. There was a considerable

scatter. Twenty-seven children excreted more than the average as against forty who excreted less. Although the proportion of the dietary thiamin excreted resembled that of the loading dose in many cases, individual variations were so great that there was no statistically significant relationship between the percentage thiamin excretion from the loading dose and that from the dietary intake in the preliminary period.

TABLE 1

AVERAGE DAILY EXCRETION OF THIAMIN EXPRESSED AS A PERCENTAGE OF THE DIETARY INTAKE

Number of cases	Range of age in years	Average percentage excretion
14	0–3	10·0
18	3–6	12·7
25	6–10	12·5
22	10–13	14·0

EXCRETION PERIOD FOR ORAL TEST. In the first forty-six tests the urine was collected for twenty-four hours in three periods of six, six and twelve hours. When the cases were grouped according to the proportion of the total excretion which occurred in the initial six- and twelve-hour periods, it was found that in only eleven cases was there at least 80 per cent. of the total excretion in the first specimen of urine (table 2).

TABLE 2

DISTRIBUTION OF CASES TO SHOW THE PROPORTION OF THE TOTAL EXCRETION FOLLOWING A TEST DOSE COLLECTED BY THE END OF SIX AND TWELVE HOURS

Percentage of total 24-hour excretion	Number of cases	
	at the end of six hours	at the end of twelve hours
Over 80	11	27
60–80	15	13
40–60	16	5
20–40	4	1

There was no relationship between the amount of the oral dose voided in twenty-four hours and the rate at which it was excreted during this period.

As the urine had to be collected for a minimum period of twelve hours following an oral dose of thiamin given with a meal in order to obtain the greater part of the vitamin excreted, urines were subsequently collected for twenty-four hours as a single sample.

A few cases received a parenteral injection of vitamin, the dose being half that of the oral. Even greater variations in the amounts excreted were noted than with the single oral dose.

TABLE 3

EXCRETION OF DIETARY THIAMIN IN CERTAIN DISEASE CONDITIONS WITH THE RESULTS OF SUCCESSIVE DAILY ORAL LOADING DOSES IN THESE AND OTHER STATES

Disease	Name	Age	Daily dietary excretion as a percentage of intake	Percentage of dose (1 mgm.) excreted on the following days															
				1	2	3	4	5	6	7	8	9	10	12	14	16	20	24	28	32
Peripheral neuritis	C. G.	4	10	9																
	J. S.	11	5	9	5	9	2	4	10	6	10	35								
	A. A.	9	20	17	8	10	31	32	29	39	35	35								
	B. G.	9	8	3	7	3	0	0	9	3	7	7	0	6	21	23	35	29		
Coeliac	R. C.	1½	8																	
	K. A.	2½	8																	
	B. B.	2	8	6	0	3	2	6	0	0	9	4	3	3	1	3	3			
	J. D.	9	10	4																
	M. W.	3	5	8																
Old coeliac	C. H.	13	38	20	13	41	31	32	56	70	26									
	G. H.	13	22	12	5	13	12	27	39	50	32	16	20	10						
Acute hepatitis	J. G.	5	47	34	60	32	34	18	33	62	72	51								
	S. H.	5	15	2	3	5	2	8	5	4	4	9	10	11	8	5	3	13	0	5
Chronic hepatitis	S. M.	12	9	0	2	12	28	23	38	54	7	51	43	37						
	B. S.	7	9	2																
	J. H.	9	11	4	0	4	20	14	12	29	26	34	21	32	30	31				
Miscellaneous																				
Diabetes	M. J.	9	9	29	36	25	26	16	29											
Empyema	G. R.	7	41	7	42	55	52	48	40	0	14	7	0	15						
Encephalitis	V. W.	7	32	23	36	50	45	49	33											
Hysteria	H. H.	13	2	18	19	31	14	17	16											
Debility	J. K.	5	30	10	26	27	28	29	19	13	13	6								
Epilepsy	F. B.	9	11	16	20	15	5	18												
Acholuric jaundice	B. A.	13	6	11	5	6	16	5	12	2	14	17	0	8	13	3				
Bronchitis	S. S.	6	8	6	16	13	7	18	8	11										
Spinal caries ..	R. W.	13	9	10	25	27	11	16	16	28	30									
Anaemia	A. S.	13	6	10	8	9	9	5	3	2										
Lacerations	P. T.	6	15	5	6	11	11	17	5	11	9									
	B. K.	11	11	0	13	15	30	8	12	7	9	10	18	16	9					

Twenty-two of the later cases received successive oral doses of vitamin daily. The resulting curves could be grouped into five types. There were eight straight-line graphs showing daily excretions of less than 13 per cent. (fig. 6). At the other extreme there were four cases showing a relatively high bi-apical curve (fig. 1), in which even the lowest point

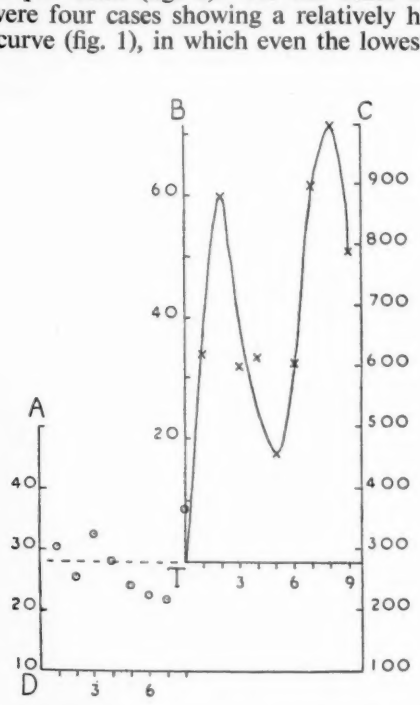

FIG. 1.—A bicuspid curve. J. G., a case of acute hepatitis.

Ordinates A. Percentage of dietary thiamin excreted. B. Percentage excretion of test dose. C. Actual daily excretion in microgm.

Abscissae D. Period of determination of dietary thiamin output in days. T. Period over which a daily test dose of 1 mgm. of thiamin was given.

of the curve was above the average excretion of the preliminary period. This configuration had previously been observed by Baucke (1939). Intermediate were eight cases giving steeply rising curves with and without an initial lag (fig. 2 and 3). In three of these cases where the dose was continued past the peak there was a rapid fall in the excretion

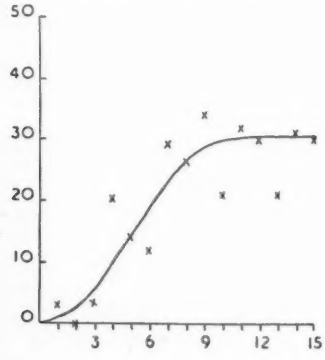

FIG. 2.—Curve showing rapid rise after an initial lag in the urinary excretion of a loading dose of 1 mgm. thiamin given on successive days. J. H., a case of hepatic cirrhosis.

Ordinates. Percentage of loading dose excreted.
Abscissae. Days.

(fig. 4 and 7). Finally there was one curve which rose only slowly after a long initial lag.

One case, C. H., with a steep curve following successive doses of 1 mgm. thiamin, received 12·0 mgm. thiamin subcutaneously on alternate days. On the day of the injection 7 to 8 mgm. was excreted. On the rest days the output was about

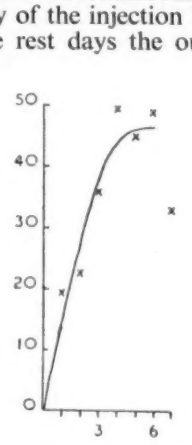

FIG. 3.—Curve showing an immediate and rapid rise following successive oral doses of 1 mgm. thiamin. V. W., a case of recent encephalitis.

Ordinates. Percentage of loading dose excreted.
Abscissae. Days.

1·0 mgm., which when compared with the average daily dietary excretion of 400 microgm. over a preliminary period of eight days, indicated a spill-over from the day before. If this single example can be taken to be representative it shows that neither the mechanism of luxury consumption (v. Drigalski, 1939) nor the renal tract can cope immediately with unphysiological doses.

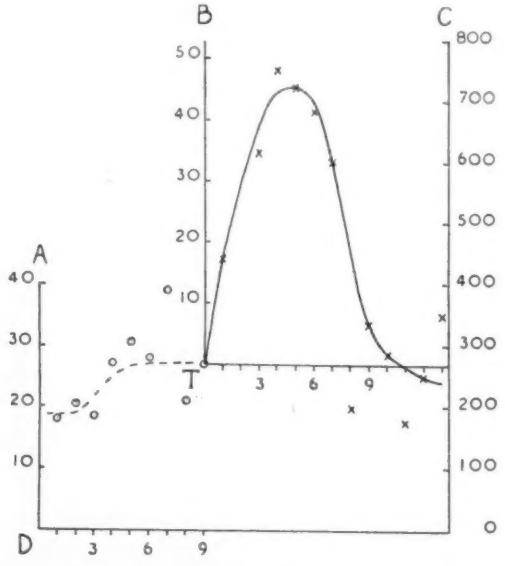

FIG. 4.—Curve showing rapid rise and fall in the excretion of thiamin following successive oral loading doses of 1 mgm. G. R., a case of recent empyema.

Ordinates A. Percentage of dietary thiamin excreted. B. Percentage excretion of test dose. C. Actual daily excretion in microgm.

Abscissae D. Period of determination of dietary thiamin output in days. T. Period over which a daily test dose of 1 mgm. of thiamin was given.

Discussion

The results of the average daily excretion of vitamin were lower than those of Benson et al. (1941), who found in healthy children an average daily excretion of 27 per cent. of the intake. The following figures compare their diets with the results of the present investigation:

	Protein (gm.)	Fat (gm.)	Carbohydrate (gm.)	Calories	Intake of B (mgm.)
Benson et al ..	85	96	236	2159	0·99
Present figures	76	94	207	1980	1·0

The discrepancy in the daily excretion is not to be explained by a difference between the calories or the calculated vitamin intake. The American children attended the hospital solely for the purpose of the test whereas ours had all been admitted for some form of therapy. Forty-seven out of seventy-nine cases had had a recent pyrexial illness, particularly the smaller children. All those in the youngest age group had been recently pyrexial. When Benson et al. (1942) also used cases which had had a recent infection they obtained lower results very similar to ours.

If the dietary excretion were estimated over consecutive days there was often a considerable fluctuation from day to day (fig. 4). The proportion of the loading dose excreted was calculated by subtracting the average dietary excretion of two or more previous days from the actual total output of vitamin. The recordings of the excretion of the loading dose were therefore modified by any variation in the dietary excretion. It follows that isolated determinations of the dietary output have a limited value and of an isolated loading dose even less. When the nutritional state of an individual is to be studied it is desirable to stabilize both diet and fluid intake. The amount of milk and bread should be constant. Other foods rich in thiamin, e.g. bacon, which tend to be given sporadically should be eliminated or given regularly. A restricted fluid intake produces a concentrated urine containing a high degree of interfering fluorescent substances which produce a high blank. Fluid in excess of normal requirements dilutes the vitamin in the urine to a degree that it is difficult to measure. It was not found that a polyuria increased the vitamin excretion. The patient should, in addition, not be receiving any absorbable drug of the sulphonamide group or salicylate. To obtain reliable results the dietary output should be estimated over a period of about a week and the loading doses for a further eight to ten days.

Sciclounoff (1939) reported four cases of vitamin B deficiency which eliminated the vitamin and two cases with no signs which excreted none. He concluded that the estimation of the urinary thiamin was not a reliable index of the degree of saturation. It is proposed to consider the results of successive oral doses in the light of this criticism.

Cases producing a rapid rise in excretion must either be near saturation point or be unable to utilize the thiamin. In the three cases G. H., G. R. (fig. 4) and J. K. (fig. 7) where the loading dose was continued past the peak excretion there followed a rapid fall in output. This may indicate that the organism had at first only a limited ability to utilize the vitamin, an improvement developing during the course of the experiment. An alternative interpretation would be that the organism adjusts itself to the overloading with vitamin by disintegrating it

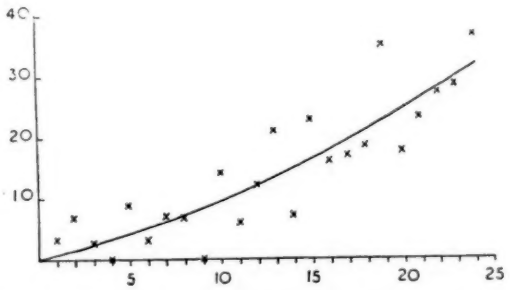

FIG. 5.—Slowly rising curve. B. G., a case of post-diphtheritic polyneuritis.

Ordinates. Percentage of oral loading dose excreted.
Abscissae. Days.

in the metabolism without using it for its physiological purpose. This phenomenon was called luxury consumption by v. Drigalski (1939). On the other hand, if one excepts the case of S. H., who had a haemolytic anaemia in addition to the hepatitis and which will be referred to later, the three other cases of hepatitis (table 3) had a persistently high excretion of the oral loading dose indicating either a persisting inability to metabolize the vitamin or a complete saturation. Similar high excretions have been observed in adult cases of liver damage (Sydenstricker, personal communication).

The eight cases, whose graph showed a straight line, all had a low excretion of 13 per cent. or less. It is probable that most of these would have eventually shown a gradual rise if continued longer, as occurred with B. G. (fig. 5). However, four cases,

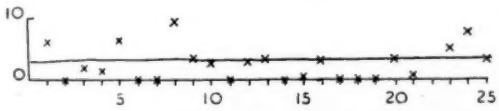

FIG. 6.—A flat curve. B. B., a case of coeliac disease.

Ordinates. Percentage of oral loading dose excreted.
Abscissae. Days.

B. K., B. A., B. B. and S. H. showed flat curves after 14, 18, 28 and 33 days respectively (fig. 6). B. B. was a coeliac and failure of absorption seemed the likeliest reason in this case. Parenteral injections were given to B. B. over consecutive days without any appreciable result during the eleven days of the test (table 4). Again the probable cause was a high degree of unsaturation consequent on failure of absorption. B. A. was a case of acholuric jaundice, S. H. a case of sub-acute atrophy of the liver complicated by the presence of pan-agglutinins acting at body temperature. In both cases there

had been, immediately prior to the vitamin assay, evidence of a haemolytic process. It is known (Sinclair, 1939) that haemin destroys thiamin. It is possible that other breakdown products of haemoglobin have a similar effect. Jansen, quoted by Schroeder (1939), considers that slight amounts of haemolysed blood cells cause the disappearance of thiamin from the blood. B. K. was a case of fractured femur, there was no apparent clinical cause for such a graph and no suggestion can be made for the low excretion in this case. A persistently low curve must mean either a failure of absorption or an increased utilization or destruction and signifies a deficiency without indicating the cause. But all the cases show that a marked unsaturation may be present without clinical symptoms of thiamin deficiency.

TABLE 4

PERCENTAGE EXCRETION OF THIOCHROME AFTER SUCCESSIVE DAILY PARENTERAL DOSES OF 0·5 MGM. VITAMIN B_1 TO A CASE OF COELIAC DISEASE

Day	1	2	3	4	5	6	7	8	9	10	11
Percentage of dose excreted ..	10	1	12	5	10	4	4	0	12	8	0

The slowly rising curves after successive loading doses also indicate a deficiency though of rather less degree. This type of curve is the most suggestive for an under saturation which becomes repaired by the intake. A similarly patterned curve may be seen during the period of determination of the dietary excretion prior to giving the loading dose (fig. 7). The rapid rise after an initial lag (fig. 2)

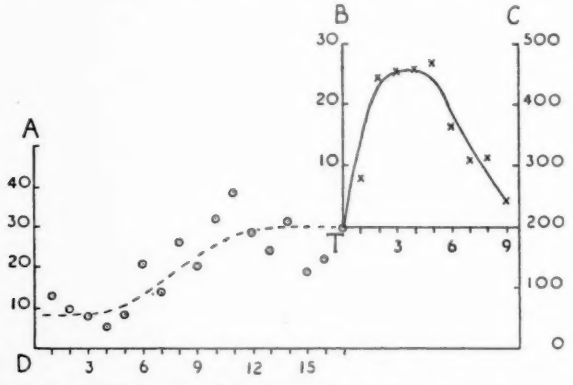

FIG. 7.—Effect of giving repeated doses of 1 mgm. thiamin after stabilisation on the ward diet. J. K., a case of debility.

Ordinates A. Percentage of dietary thiamin excreted. B. Percentage excretion of test dose. C. Actual daily excretion in microgm.

Abscissae D. Period of determination of dietary thiamin output in days. T. Period over which a daily test dose of 1 mgm. of thiamin was given.

also suggests a deficiency (Wang and Harris, 1939), though naturally less severe than in the case of the slowly rising curve. In the case J. H., shown in fig. 2, the dietary excretion had been determined for only two days prior to giving the loading doses and averaged 11 per cent. of the intake. It seems likely that if no loading doses had been given until dietary stabilization had occurred, a graph similar to that seen in fig. 7 would have resulted.

Within the limits above defined, the oral loading dose applied over successive days may give information as to whether the body has been absorbing the optimum amount and whether it is capable of utilizing it. To this extent it is not possible to agree with the views of Sciclounoff. No claim is made that the test gives any indication of the clinical state. In the present series no case of beri-beri was recognized, though it is interesting to speculate whether the cases of peripheral neuritis owed a degree of their severity to a previous subclinical deficiency.

It is probable that the body can adjust itself to wide ranges of intake. Meyers (1941) found in the Javanese on a high carbohydrate diet of polished rice with little fat that the average urinary excretion of thiamin was low though beri-beri was rare. He suggested a possible adaption to a long-standing low vitamin B intake for the low incidence of clinical deficiency.

A further explanation of anomalies between the amount of intake and the presence and severity of symptoms is the formation of vitamin by biosynthesis. Najjar and Holt (1943) found that four out of nine individuals on a thiamin free diet did not develop beri-beri and that these four excreted considerably more free thiamin in the stools than did the five with symptoms of beri-beri. This faecal excretion diminished when the bacterial flora was reduced by succinyl sulphathiazole.

The above points, coupled with the English standard of living, are sufficient to explain the rarity of symptoms suggesting a deficiency.

Summary

The results of the estimation of urinary thiochrome in a group of eighty children are described.

The relative value of estimations of dietary excretion and following isolated and consecutive loading doses of thiamin is discussed.

Although many recently ill children excreted reduced amounts of thiamin no symptoms which could be directly attributed to beri-beri were found even in the most severely depleted.

Thanks are due to Prof. L. G. Parsons, Dr. E. M. Hickmans and to Dr. H. S. Baar for their kind help and advice, and to the Honorary Staff of the hospital for permission to use their cases. One of us (E. F.) was in receipt of a grant from the Medical Research Council which has also defrayed the expenses of the laboratory work.

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CASE REPORTS

IDIOPATHIC MUSCULAR HYPERTROPHY OF OESOPHAGUS, PYLORUS, DUODENUM AND JEJUNUM IN A YOUNG GIRL

BY

KATHARINE J. GUTHRIE, M.D.

(From the Department of Pathology, Royal Hospital for Sick Children, Glasgow)

The condition here described is of interest on account of its extreme rarity, no record of exactly similar findings having been discovered in a fairly exhaustive search of the literature. Two illustrations are appended (fig. 1 and 2).

The patient, J. McH., a girl aged eleven years, the first-born in the family, who had previously been healthy, was admitted on 11.2.42 with a history of illness of a few days' duration beginning abruptly with bilious vomiting and green diarrhoea, followed by severe abdominal pain and after a short interval by a convulsion. The child lapsed into coma and was unconscious on admission, with intermittent spasticity of the limbs and rotary nystagmus. The urine contained albumin with a trace of acetone. The blood non-protein nitrogen was 125 mgm. per 100 c.cm. There was no oedema. Death occurred about twelve hours after admission.

An autopsy was performed some nine hours later. The girl was well-grown and of normal build with no excessive muscular development or other external feature of note. Acute nephritis was the cause of death and there was an early broncho-pneumonia. The left ventricle was slightly hypertrophied. Apart from the renal lesion no morbid change was observed in the solid abdominal organs which were all of normal size. On opening the abdomen, a striking feature was the condition of the alimentary tract. The distended stomach had a rather thin wall, except in the pyloric canal which showed massive muscular hypertrophy. The calibre of the duodenum and jejunum was greatly increased and the wall so thick that on palpation it felt like heavy rubber tubing. The small bowel gradually decreased in size from above down and reached normal dimensions in the terminal ileum. There was no abnormality of the ileo-caecal valve or of the colon. On examining the pharynx and oesophagus no pharyngeal lesion was found and the oesophagus was normal in its upper third. The lower two-thirds where the muscle is non-striated had assumed the form of a thick-walled tube of rubber-like consistency as a result of muscular hypertrophy of the wall, fairly uniform throughout although tending to increase slightly towards the lower end, and ceasing abruptly at the cardia where there was no sign of any obstruction. The gullet was not dilated, the condition being one of pure hypertrophy.

On slitting open the alimentary tract, the thickened muscle was rather paler than usual but otherwise appeared healthy. The mucosa lining the oesophagus, stomach and intestines was smooth, glistening and free from any appearance of morbid change. In the hypertrophied areas, i.e. the lower oesophagus, the pylorus, duodenum and upper jejunum, it was considerably thickened with unusually prominent rugae. These encroached to some extent on the lumen of the oesophagus and pylorus. Measurements of the outer circumference and parietal thickness of the oesophagus, pylorus, duodenum and ileum were made at various levels before fixation. These are tabulated below, with

FIG. 1.—Muscular hypertrophy of lower end oesophagus, pyloric canal and duodenum.

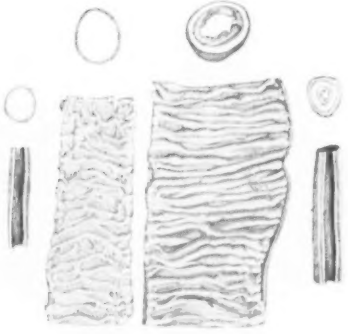

FIG. 2.—Muscular hypertrophy of mid-oesophagus and jejunum. These are seen slit lengthwise and in cross-section. The normal-sized oesophagus and jejunum from a child of the same age are shown for comparison.

normal figures for comparison from a child of approximately the same age.

	J. McH.		Normal	
	Circumference	Thickness of wall	Circumference	Thickness of wall
Oesophagus	5·8 cm.	6 mm. (mid $\frac{1}{3}$) 8 mm. (lower $\frac{1}{3}$)	5 cm.	2 mm. (mid $\frac{1}{3}$) 2 mm. (lower $\frac{1}{3}$)
Pylorus ..	9·7 cm.	1 cm.	7·5 cm.	3 mm.
Duodenum	10 cm.	5 mm.	7·5 cm.	2 mm.
Jejunum (upper) ..	7·5 cm.	5 mm.	4·5 cm.	2 mm.
Ileum (lower) ..	4·2 cm.	3 mm.	3·5 cm.	2 mm.

In view of these autopsy findings the parents were asked if the child had ever had dysphagia or any abnormal feeding habits, e.g. excessive appetite, since the large size of the upper intestinal coils recalled Saint-Simon's account of the post-mortem on Louis XIV, ' The capacity of the stomach and intestines was at least double that of men of his height which was extraordinary and was the cause of his being such a constantly great eater.' No such history was forthcoming in the present case. The child's appetite had never been excessive and there had been no difficulty in swallowing and no vomiting apart from an occasional ' bilious attack.' The severe attack of vomiting beginning a few days before death was in all probability a uraemic manifestation.

Histological examination showed an identical picture at various levels throughout the oseophagus, pylorus, duodenum and jejunum, the essential abnormality consisting in massive hypertrophy of the circular (inner) muscle coat which in all these regions formed a broad continuous band approximately three to four times the thickness of the longitudinal layer which itself was moderately hypertrophied. Normally these coats are about the same thickness. Hypertrophy of the circular muscle in the intestine gradually diminished distally till, in the terminal ileum, whilst the muscle coats were still slightly thicker than usual, they were restored to approximately equal width. Below the ileo-caecal valve muscular thickening had disappeared. In the oesophagus the muscularis mucosae was rather more prominent than usual but elsewhere there was no noteworthy over-development. The individual muscle cells were free from degenerative change. In the interstitial tissue between the muscle bundles and also in the plane between the circular and longitudinal muscle coats, where they were chiefly perivascular, there occurred small collections of inflammatory cells, chiefly polymorphonuclear and eosinophil leucocytes. This focal infiltration was obviously a recent event and may be considered merely incidental. There was no trace of chronic inflammatory change in the form of connective tissue overgrowth anywhere in the wall in any of the numerous sections examined, the condition being one of pure muscular hypertrophy without an inflammatory component. The myenteric nerve plexuses with their ganglion cells remained in a state of good preservation, free from atrophy or fibrosis. There was slight widening of the submucosa which presented no feature of special note except that some of the smallest arterioles tended to be rather thick walled. The other blood vessels were normal. The oesophageal epithelium was of ordinary squamous type. Sections of the kidneys showed typical acute glomerulo-nephritis.

Discussion

Idiopathic muscular hypertrophy occurring in the alimentary tract is rare.

Helmke (1939), in recording four cases of muscular hypertrophy of the oesophagus, could find only eight other reports in the literature, those of Pitt (1888), Rolleston (1899), Elliesen (1903), Ehlers (1907), Rake (1926), von Brücke (1928), Goedel (1929) and Wood (1932). Another probable example of this condition, however, is included by Baillie (1799) in his list of engravings. In the case reported by Reher (1885) hypertrophy of the oesophagus was found in a man who died of rectal carcinoma. The gullet was not examined histologically so that carcinomatous involvement could not be excluded with certainty. Hypertrophy of the oesophagus, sometimes combined with that of the pylorus and terminal ileum, is described also in the horse but in no other animal (Kitt and Dobberstein 1939, quoted by Helmke). The cases mentioned above, exclusive of Baillie's of which no clinical description is extant, were all adults between the ages of 39 and 69 years, and all male with the single exception of a 68-year-old woman. Muscular thickening was confined to the oesophagus except in Ehler's case and in one of Helmke's, where hypertrophy of the pylorus was present in addition. Specimens from an infant aged 3 months showing hypertrophy of the lower end of the oesophagus, of the pylorus and ileo-caecal sphincter, were shown at a meeting of the Royal Society of Medicine by Pritchard and Hillier (1920). This case, in point of age and multiple involvement of smooth muscle, bears the closest resemblance to the one under discussion, in which marked oesophageal hypertrophy occurring in a young girl was associated not only with great thickening of the pyloric muscle but with the unusual condition of gigantism affecting several feet of the duodenum and jejunum. Not only was the calibre of the bowel greatly increased but the wall was markedly hypertrophied. Diminution both in girth and in parietal thickness distally was very gradual. There was no evidence of obstruction at the cardiac, pyloric or ileo-caecal sphincters.

From the scarcity of references idiopathic enlargement of the small bowel appears to be very rare. Torkel (1905) describes cylindrical dilatation of a segment of jejunum which he regards as a congenital malformation of unknown cause. Melchior (1924) and Judd (1921) quoted by Melchior, report cases involving the duodenum and upper jejunum without mechanical cause, and Hunter (1933) found localized idiopathic dilatation of the duodenum and ileum in a still-born infant. During his investigation on benign hypertrophy of the adult pylorus, which he found not infrequently, Rössle (1935) encountered idiopathic muscular hypertrophy of the jejunum in an elderly man, and of the lower ileum and pyloric antrum in a young woman with otherwise poor muscular development.

All the authors who record adult cases of oesophageal hypertrophy agree closely in their description of the condition. The lower part of the oesophagus is uniformly thickened, with some encroachment on the lumen. There is no dilatation. The consistence of the wall is tough and leathery so that the viscus cuts with difficulty and sometimes creaks under the knife. No obvious sign of disease is visible in the hypertrophied muscle coats of which the circular is chiefly involved, reaching several times the thickness of the longitudinal. Muscular hypertrophy is sometimes very great, reaching a maximum in von Brücke's case in which the wall was 15 mm. thick. Arnold (1932–33) gives the normal figure as 3 mm. of which the muscle forms the largest part. In the case under discussion the wall of the gullet was 8 mm. thick near the lower end.

Hypertrophy of the circular muscle without noteworthy participation of the other muscular coats in the wall of the oesophagus may result from the fact that the various muscle layers appear independently at different stages of embryonic development. The circular muscle, according to Harris (1929), is present in the 12 to 17 mm. embryo, while the longitudinal coat is not evident till the 55 mm. stage. The muscularis mucosae appears still later at 90 mm.

Except in Rake's case, where inflammatory change at the lower end of the gullet involved all tissues including Auerbach's plexus, no histological evidence of inflammation, old or recent, nor of other morbid change was found in the muscle coats, of which the individual fibres were essentially normal. Von Brücke describes slight cell-infiltration in the septa between the muscle bundles and round the blood vessels in the plane between the muscle coats as in the present case, but does not consider it indicative of an inflammatory basis for the muscular hypertrophy. Wood states that the nerve ganglia were normal in his case. The integrity of the myenteric nerve plexuses and their ganglion cells in the present case supports the view that muscular hypertrophy is purely of the nature of an overgrowth—a condition of localized gigantism—and not a disease process. As previously mentioned the ganglion cells are described as atrophied and fibrosed in achalasia of the cardia with subsequent oesophagectasia.

Clinical information in recorded cases of oesophageal hypertrophy usually mentions no symptoms during life to suggest a lesion of the gullet. Elliesen's patient, however, a man aged 39, had been obliged since the age of fifteen years to chew his food thoroughly though he had never failed to swallow it. Presumably an attack of dysphagia had occurred at the age of fifteen, but no information is forthcoming as regards its nature. The present case is similar to those quoted in having no clinical symptoms during life to suggest any oesophageal abnormality. In a number of the recorded cases death was due to chronic nephritis with considerable hypertrophy of the heart, and Helmke suggests that muscular hypertrophy of the lower oesophagus may have developed in the attempt to overcome the pressure exerted by the enlarged heart. Most authors, however, can find no explanation for the condition and regard it as idiopathic or congenital.

The present case and that of Pritchard and Hillier tend to confirm the idea of congenital origin, since in both there occurred in early life marked overgrowth of non-striated muscle without obvious cause at various levels in the alimentary tract. In Elliesen's patient the history suggests that an oesophageal abnormality already existed in early adolescence. In the absence of clinical symptoms in the other recorded adult cases it is impossible to determine the duration of oesophageal hypertrophy.

Summary

An unusual juvenile case is reported of symptomless idiopathic and possibly congenital muscular hypertrophy of the oesophagus, pylorus, duodenum and jejunum.

Thanks are due to Prof. G. B. Fleming for permission to make use of the case record, and also to Mrs. Hamilton (C. Brown Kelly) for the drawings.

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CYSTIC FIBROSIS OF THE PANCREAS

BY

W. DOUGLAS HENDERSON, M.B., F.R.C.P.Ed.

Hon. Physician, Woking Victoria Hospital

Passini (1919) was apparently the first to describe a case of faulty digestion in an infant due to pancreatic disease, and it would appear from a brief survey of the literature that not many cases of cystic fibrosis of the pancreas have been reported in this country, whereas in the United States, since Andersen (1938) correlated the pancreatic changes with steatorrhoea and pneumonia to form the syndrome of cystic fibrosis, many more cases have been reported. Menten and Middleton (1944) suggest that there is a significant increase in this disease.

Wolman (1942), in an excellent review of the literature, points to the importance of differential diagnosis from coeliac disease, and this case is reported to show some of the difficulties of diagnosis before death.

Case history

M. K., a male child aged twenty-two months, was admitted to the Woking Victoria Hospital on April 4, 1945, giving a history of not gaining weight and passing frequent large and offensive stools. At birth he weighed 7 lb. 13 oz. and was breast fed for five weeks. He always appeared hungry and the feed was changed to a dried milk. He then gained normally until he was one year old, when he weighed 21 lb. He had had a big abdomen and an abnormal appetite from birth. There were no previous illnesses and it was particularly determined that the child had never had a cough. He could not tolerate war-time concentrated orange juice and cod-liver oil was not well taken. At fifteen months diarrhoea started with large, oily stools, seven to eight a day.

The mother is apparently healthy and no relevant medical history could be obtained. The father is stated to have been a premature baby, was jaundiced at birth and did not walk till he was three years old, having worn calipers until then. There is one other child, a girl aged nine months, who is apparently perfectly healthy.

On admission the child weighed 24 lb. and was definitely under-nourished, with a protruberant abdomen. Muscle wasting was not prominent. Clinical examination showed all organs apparently healthy, but the stools, which were large, pale, offensive and of a soft, greasy consistency, were passed up to seven or eight times a day. The Vollmer tuberculin patch test was negative.

In spite of the appetite, which was enormous (the child was crying for food all day) a provisional diagnosis of coeliac disease was made and appeared to be borne out by a fat estimation of the stool. This, on April 5, showed that, of the dried faeces:—

Total fat	65·8 per cent.
Neutral fat (unsplit)	7·5 ,, ,,
Fatty acids	58·3 ,, ,,

(of the faecal fat, 88·6 per cent. was split).

There was still a doubt as to the true nature of the disease and it was decided to carry out vitamin A absorbtion tests and glucose tolerance tests. Before these could be done the child developed measles and on April 18 the weight had dropped to 22 lb. 7 oz; it was therefore decided to begin treatment at once with liver extract and vitamin B complex, as recommended by Paterson et al. (1945). The preparation used was Heparglandol (Roche) and seven injections on alternate days were given intramuscularly.

On April 27 a further fat estimation of the stool showed a fall in the fat content, the figures being:—

Total fat	34·5 per cent.
Neutral fat (unsplit)	10·7 ,, ,,
Fatty acids	23·8 ,, ,,

(of the faecal fat, 69 per cent. was split).

At this stage the child developed broncho-pneumonia and became seriously ill. Treatment with Heparglandol was stopped and chemotherapy was commenced. It was noted that sulphamezathene and sulphathiazole had no effect upon the course of the pneumonia, whilst sulphadiazine had a slight effect only. A course of penicillin, 15,000 units three-hourly, was then tried, but had no effect on the lung condition, and death took place on May 29.

A third fat estimation had been done on May 19 and there was again an increase:—

Total fat	56·1 per cent.
Neutral fat (unsplit)	10·4 ,, ,,
Fatty acids	45·7 ,, ,,

(of the faecal fat, 81·4 per cent. was split).

Post-mortem report. The body was that of a thin, emaciated child, with a distended abdomen. The liver was found to be slightly enlarged and showed a pale cut surface. The stomach and intestines were normal, but the mesenteric glands were large. The pancreas was long and thin and pink in colour. It was adherent to surrounding structures and felt hard and nodular. The lungs showed areas of collapse and consolidation and a thin mucopus could be expressed from the bronchioles. All other organs were healthy.

Histological report

PANCREAS. Cystic fibrosis. No evidence of acute or chronic inflammation. Fibrous tissue was greatly in excess with swollen acini scattered throughout. The acini were filled with a pink eosin staining substance (fig. 1).

LIVER. Acute venous passive congestion.

MESENTERIC GLANDS. Chronic lymphadenitis.

Discussion

Blackfan and May (1938) state that the clinical manifestations of cystic fibrosis of the pancreas are limited in variety, but are so common to many disorders of infancy that it has not been found possible to determine accurately the dependable diagnostic features. On the other hand, Kennedy and Baggenstoss (1943) give the following features, which go to make the diagnosis of cystic fibrosis: the combination of steatorrhoea, chronic cough and absence of trypsin.

It is regretted that in this case there had been no estimation of trypsin, but even so the difficulties of diagnosis are borne out. It is here shown that estimations of the fat content of the stool cannot establish the diagnosis, as the figures show what would appear to be a typical case of coeliac disease.

Theoretically, an absence of pancreatic lipase will lead to an increase in neutral unsplit fats in the stool, but this has not been borne out in practice, as in this case, in which there was a constantly high percentage of split fats, and all the while the child was under observation it had been fed on a normal diet.

Deem and McGeorge (1941) point out that the concentration of fat in the stool depends on the diet and it has been suggested that where there is a high percentage of fatty acids, the fats in the diet have been split, presumably by lipase of the intestinal juice.

In spite of the absence of definite evidence of pancreatic activity in this case, it is difficult to assume that the fat from a normal diet could have been acted upon by lipase from the intestinal juice alone, to such an extent as to give so high a percentage of split fats, and it must be assumed that a good deal of the remaining acinar tissue of the pancreas must have been in an active state and that there was free exit from the gland to the intestine so that the ferment could digest the fats. Thus it must be reasonable to assume that there is a normal or increased secretion of fat digestants from the pancreas.

Menten and Middleton (1944) report eighteen cases with diffuse definite dilatation of pancreatic acini and associated pneumonia. They state that radiological examination of the lungs in their cases showed remarkable similarity in the unusual enlargement of hilar shadows and a bilateral shadow decreasing to the periphery and suggest this as a diagnostic feature.

Snelling and Erb (1942) had also found that physical signs of lung involvement such as bronchitis, collapse and consolidation of the lung, broncho-pneumonia and bronchiectasis were present on admission or during the period of observation in all their nineteen cases.

No evidence of lung involvement could be found in the present case to support these contentions, apart from some enlargement of the hilar shadow; this latter was not really excessive, although radiological examination of the chest was not done until May 14, after the pneumonia had developed.

Points in the diagnosis of cystic fibrosis are: (i) early age of onset; (ii) steatorrhoea associated with a large appetite; and (iii) ? absence of pancreatic enzymes obtained by duodenal intubation. Treatment with vitamin A and pancreatin has been tried in many cases, but the results have been too indefinite to be of value and at present treatment of

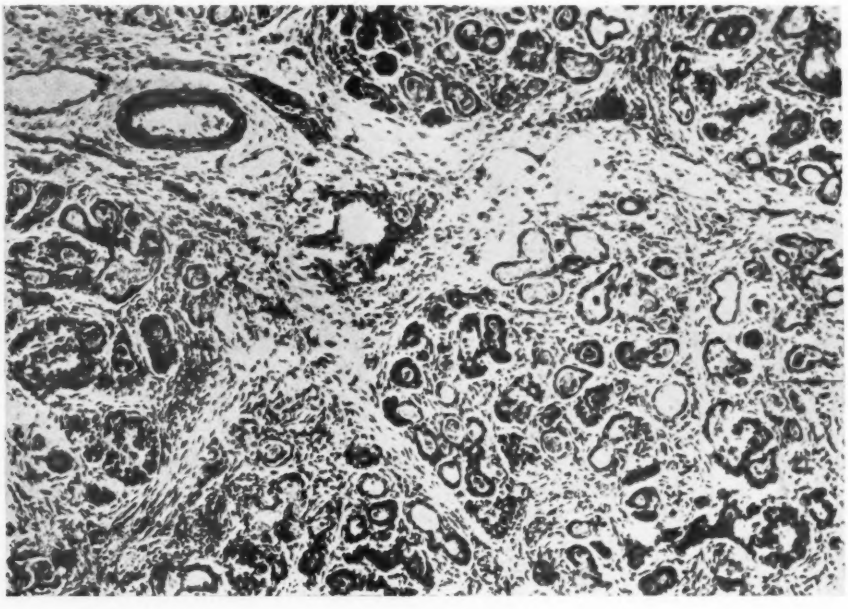

FIG. 1.—Section of pancreas showing cystic acini and excess of fibrous tissue. (Haem. and Eosin.)

the disease can only be considered as hopeless. It might be worth while to consider treatment with liver extract and vitamin B, as it was noted that there was a drop in the fat content of the stool after seven injections of Heparglandol.

Thanks are due to Dr. D. C. L. Derry and Dr. Griffiths of Botley's Park E. M. S. Hospital, for their reports on the pathological specimens and fat estimations respectively.

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BRITISH PAEDIATRIC ASSOCIATION

PROCEEDINGS OF THE SIXTEENTH ANNUAL GENERAL MEETING

The Sixteenth Annual Meeting of the British Paediatric Association was held at Rugby School, by kind permission of the head master, P. H. B. Lyon, Esq., M.A., on August 2 and 3, 1945.

Business proceedings: The President, Prof. L. G. Parsons (Birmingham), was in the Chair and the following members were present:

Drs. H. Ashby, G. Bray, W. Brown, H. C. Cameron, N. Capon, R. W. B. Ellis, G. Fleming, F. J. Ford, A. W. Franklin, W. Gaisford, C. K. J. Hamilton, C. F. Harris, R. Hutchison, C. P. Lapage, A. G. Maitland-Jones, C. McNeil, A. Moncrieff, D. Nabarro, A. Naish, A. V. Neale, A. Ogilvie, D. Paterson, W. Payne, C. B. Perry, C. Potter, B. Schlesinger, J. W. Scott, W. Sheldon, A. Hayes Smith, R. E. Smith, J. Spence, R. E. Steen, R. R. Struthers, K. Tallerman, W. Vining, J. F. Ward, A. G. Watkins, K. D. Wilkinson, T. P. Williams, D. W. Winnicott. There were 14 guests.

Apologies for absence were received from the following: Drs. F. Allen, C. Box, T. Y. Finlay, H. M. Fletcher, N. Hobhouse, James Hutchison, R. Jewesbury, R. Lightwood, L. Nicholson, J. Smellie, L. Thatcher, L. Walker and W. G. Wyllie.

The Minutes of the last Annual General Meeting were approved and signed by the Chairman. It was noted that all matters arising out of the Minutes of that meeting had since been dealt with.

The Secretary's Report on the activities of the Association since the last annual meeting was received and approved. It was noted that it was to form the basis for the after-dinner discussion 'The Activities of the Association—Past, Present and Future.'

The report of the Treasurer was received and approved. It was noted that the cash balance in hand was £109 10*s*. and that expenditure during the preceding two years had been £222 0*s*. 8*d*. It was therefore proposed that, owing to the increased activities of the Association and resulting increase in expenditure, the Annual Subscription be increased from £1 to £2 per annum.

Alterations to the rules of the Association: Dr. A. Moncrieff, on behalf of the Executive Committee, spoke to the motion 'That the Rules of the British Paediatric Association be altered in accordance with the document circulated.' The suggested alterations were approved subject to certain alterations in wording.

Election of officers: The President informed the meeting that since the circulation of the Ballot Paper, Dr. Lewis Thatcher had withdrawn his name. The Executive therefore recommended that Dr. H. L. Wallace's name be inserted on the Ballot Sheet in lieu.

The following were then unanimously elected by ballot as officers for the year 1945/46:

President: Prof. Geoffrey B. Fleming, Glasgow.

Joint Hon. Secretaries:
Dr. Donald Paterson, London, and
Dr. Alan Moncrieff, London.

Hon. Treasurer: Dr. Donald Paterson, London.

Executive Committee:
LONDON: Dr. Charles Harris.
Dr. R. W. B. Ellis.
PROVINCES: Prof. C. Wilfred Vining, Leeds.
Prof. C. Bruce Perry, Bristol.
SCOTLAND: Dr. H. L. Wallace, Edinburgh.
IRELAND: Dr. F. M. B. Allen, Belfast.

Election of new members: The following were elected to Membership of the Association, by Ballot:

HONORARY MEMBERS:
Dr. John Murray Bligh, Liverpool.
Dr. Catherine Chisholm, Manchester.
Mr. H. A. T. Fairbank, London.
Sir John Fraser, Edinburgh.
Sir Wilson Jameson, London.
Sir Edward Mellanby, London.
Professor Leonard Parsons, Birmingham.
Dr. E. Bellingham Smith, London.

CORRESPONDING MEMBERS:
Dr. William Emdin, Cape Town, S. Africa.
Dr. F. F. Tisdall, Toronto, Canada.

ORDINARY MEMBERS:
Dr. Frances Braid, Birmingham.
Mr. Denis Browne, London.
Dr. W. H. P. Cant, Birmingham.
Dr. Beryl Corner, Bristol.
Mr. James Crooks, London.
Dr. George Davison, Newcastle.
Dr. P. R. Evans, London (on active service).
Dr. Ian Gordon, Aberdeen (on active service).
Dr. H. H. Chodak Gregory, London.
Dr. John Duncan Hay, Liverpool (on active service).
Dr. J. L. Henderson, Edinburgh.
Mr. T. T. Higgins, London.
Dr. D. V. Hubble, Derby.
Dr. Helen Mackay, London.
Dr. G. H. Newns, London.
Dr. John N. O'Reilly, London.
Dr. Charles Pinckney, London.
Dr. A. Gordon Signy, London.
Dr. J. Forest Smith, London.
Dr. Magnus L. Thomson, Manchester.

Next place of meeting: It was Resolved that this be left in the hands of the Executive Committee, but that the possibility of a May meeting at Windermere might be borne in mind.

Scientific film association: A questionnaire asking for suggested titles for medical films for (a) Students and (b) the general public had been circulated. Members were requested to hand in their completed questionnaire.

Journal of Pediatrics: Dr. Borden Veeder had kindly offered an unbound volume of the *Journal of Pediatrics* to be presented to any medical school or hospital that lost such journals as the result of enemy action. Members were asked to intimate if they wished to avail themselves of this offer.

REPORT OF THE SECRETARY ON THE ACTIVITIES OF THE EXECUTIVE COMMITTEE FROM DECEMBER, 1943, TO JULY, 1945.

Since the last General Meeting held on December 11, 1943, at the Royal Society of Medicine, your Executive Committee has met on ten occasions.

1. **Height-weight survey:**, Your Executive Committee endeavoured to secure financial support from the Science Committee of the Royal College of Physicians in the first instance, without success; latterly the Halley Stewart Trust and the Nuffield Trust have been approached and the matter is still under consideration by the Trustees.

2. **Rheumatism report:** A final joint report on 'The Care of the Rheumatic Child,' was published in the

medical press, a copy of which was circulated to all members.

3. **B.M.A. and *Archives of Disease in Childhood*:** Members of the Association will be gratified to see that the Archives now incorporates the *British Journal of Children's Diseases* and that the B.P.A. is mentioned on the cover of the Journal. The Editorial Committee has been revised and this Committee is now appointed jointly by the B.P.A. and the B.M.A. In this way your Association is officially associated for the first time with the management of this Journal.

4. **Government White Paper on a comprehensive medical service:** Your Representative (Dr. Donald Paterson) has on several occasions attended meetings at the Royal College of Physicians of the Consultant Services Committee, and you are aware of the progress made in these deliberations. Members of the Association will realize that the Association will be consulted more and more in matters pertaining to a Paediatric Health Service in the future, as the scheme for a Comprehensive National Health Service matures.

5. **Tuberculosis report:** You have received a copy of the booklet entitled 'Childhood Tuberculosis—a word for the Health Visitor' from the B.P.A. and the N.A.P.T. This was based on the Association's report on 'The Early Diagnosis of Tuberculosis in Childhood' which you had previously received. The Chairman of the Sub-Committee on Tuberculosis, Dr. W. Sheldon, continues as the Association's representative on the Joint Tuberculosis Council, and he was largely responsible for preparing the text of the booklet referred to above.

6. **Public Health Committee of the B.M.A.:** In January of this year your President, Dr. L. G. Parsons, was adopted as the B.P.A's. Representative to this Committee. The Association will no doubt be gratified to note that at last the B.M.A. has recognized something of the importance of paediatrics by co-opting a member of the B.P.A. to this Committee.

7. **Child Guidance Council:** Dr. Charles Harris is serving as your Representative on this Council.

8. **Rickets report:** Following the publication of the report on 'The Incidence of Rickets in War-Time' (H.M. Stationery Office, Report on Public Health and Medical Subjects, No. 92) your Association was asked to prepare a leaflet suitable for distribution to Medical Officers of Health and other Public Health Workers. This was undertaken for the Association by Dr. Kenneth Tallerman and a copy of this leaflet will shortly be circulated to all members.

Your Executive has already been asked by the Ministry of Health for its views on the unsatisfactory 'take-up' of the Government Vitaminised Oil and Fruit Juice. A questionnaire has been sent to all members on this subject, the results of which are being analysed.

9. **Ministry of Education:** An inquiry was received from the Ministry of Education regarding 'Routine Medical Inspection of School Children,' a copy of which was circulated to all members; replies were analysed and a copy of the final views expressed on your behalf by the Executive Committee, as sent to the Ministry of Education, was circulated to all members.

10. **Nomenclature of disease:** At the request of the Royal College of Physicians, Dr. Norman Capon was appointed your Representative to undertake the revision of the sections of this publication relating to Paediatrics.

11. **Continental child relief:** The Chairman of your Sub-Committee, Dr. R. Lightwood, has submitted reports at intervals and has kept in touch with Representatives of U.N.R.R.A. and the Save the Children Fund. The Association has acted in a Consultative capacity to the latter organization. Dr. R. R. Struthers, corresponding member of the B.P.A., has attended meetings of the Executive Committee on behalf of U.N.R.R.A. from time to time, and has kept us informed of the state of affairs regarding children on the Continent.

12. **Hospital architecture and the part it plays in the prevention of cross-infection in children's hospitals, etc.:** The problem is so complex and difficult a matter to deal with that it has taken your Sub-Committee, under the Chairmanship of Dr. A. G. Watkins, much time and thought to plan the scheme for their report. Various members of the profession have been co-opted to assist with this report, and a long-term Ward Diary to record cross-infections from day to day has been drawn up.

13. **Child psychology:** This subject has proved a most controversial one, and the various members of the Sub-Committee were unable to agree on detail to any extent. It was therefore decided to form a new Sub-Committee, under the Chairmanship of Dr. W. G. Wyllie and comprising in addition Drs. Charles Harris and C. T. Potter, with power to co-opt others. The Terms of Reference to be: 'To examine and inquire into the existing facilities for the diagnosis and treatment of psychological problems in childhood, and the character of the work undertaken in such places as are provided.' It is hoped to have this report in your hands in the near future.

14. **Vitamin preparations:** Members will remember at the last General Meeting you were informed that Dr. Cecile Asher had undertaken to produce a report showing the vitamin content of proprietary preparations. A copy of this report, prepared for your Association and published in the *Practitioner* has been circulated to all members. Dr. Cecile Asher has been thanked on your behalf for this valuable contribution.

15. **Neonatal mortality:** A Joint Committee, comprising representatives of your Association and the Royal College of Obstetricians and Gynaecologists has met on several occasions under the Chairmanship of Mr. Eardley Holland. A draft report, prepared by a sub-committee comprising Mr. Eardley Holland, Dr. A. White Franklin, Dr. Alan Moncrieff and Mr. W. C. W. Nixon was submitted to the Joint Committee; a further revision and re-drafting of the report has been left in the hands of Prof. Norman Capon and Mr. T. N. A. Jeffcoate, both of Liverpool. Part of the revised report has already been considered by the Joint Committee.

16. **Bureau of Nutrition Surveys:** This Bureau, under the Directorship of Prof. Marrack, London Hospital, was formed on March 29, 1944, its objects being: 'To advance the science of Nutrition, to initiate or indicate, but not to undertake, lines of research; to stimulate the diffusion of the knowledge of nutrition amongst all classes of Society.' Dr. W. W. Payne was elected your Representative on the Scientific Sub-Committee and Dr. Kenneth Tallerman on the Clinical Sub-Committee of this Bureau.

17. **National Association of Maternity and Child Welfare Centres.** (Annual Meeting June, 1945.) Dr. Alan Moncrieff represented the Association and took part in a Discussion on 'The Importance of Maintaining the Unity of the Maternity and Child Welfare Services.'

18. **Royal College of Obstetricians and Gynaecologists:** Members will be pleased to learn that the President of your Association, Dr. L. G. Parsons, was elected an Honorary Fellow of the Royal College of Obstetricians and Gynaecologists.

19. **Chair of Child Health:** Members of the Association will be pleased to recall that a Chair of Child Health was instituted at Liverpool and that one of the members of the B.P.A.—Dr. Norman Capon—was appointed its first Professor.

20. **Post-war convalescent homes:** Arising out of a suggestion by Dr. Wilfrid Sheldon, the Association has met Representatives of the I.C.A.A. on several occasions, and your Executive has appointed Representatives of your Association to a Standing Joint Committee on Convalescent Homes, with Representatives of the I.C.A.A. and Hospital Almoners' Association; your Representatives are Drs. Paterson, Sheldon and R. E. Smith. The Objects of the Sub-Committee are: 'The inspection of Convalescent Homes; advice on the open-

ing of new homes, and preparation of a brochure in which homes which have been inspected should be indicated.'

21. **Paediatric Committe of the Royal College of Physicians:** Members have received a copy of the Interim Report of this Committee dealing with the first part of the Terms of Reference, namely, 'To inquire into the education of undergraduates and postgraduates in the subject of Infant Hygiene and Diseases of Children.' The second part of the Terms of Reference 'to make recommendations covering this branch of medical practice in the future' is being considered by the Committee and your Executive Committee is preparing a Memorandum on the subject of a National Paediatric Service for submission to the College Committee.

22. **Post-war planning for hospitals:** Members will have noted in the Medical Press that Representatives of the Association visited Wolverhampton on March 16 and 17 to advise on the post-war planning of the Paediatric Services associated with the Royal Hospital, Wolverhampton. Since that date the Association has been asked to send Representatives to advise in a similar capacity to the Worcester Royal Infirmary and to the Royal Devon and Exeter Hospital; these visits have been arranged for July 20 and 21 and August 17 and 18, respectively.

Such visits are of considerable educational value both to the Association's members and the Hospital visited; they are to be welcomed and it is to be hoped that other areas will call on the Association in a similar advisory capacity.

23. **Comprehensive training for State registered children's nurses:** The General Nursing Council is engaged in the revision of the training of all nurses, including children's nurses. Your Executive Committee has interested itself in this subject and has prepared a Memorandum (a copy of which you have received) dealing with certain general principles in the training of the State Registered Children's Nurse; copies of this Memorandum have been forwarded to the General Nursing Council. It is hoped that representatives of your Association will be invited to attend the Education Committee of the G.N.C. to discuss the subject at the appropriate time. In the course of its deliberations on this subject your Executive met representatives of the Association of Sick Children's Nurses.

24. **Gift.** A gift of £25 has been received from Dr. C. Paget Lapage, and with your permission the Executive Committee propose to allocate this for a signed review on 'Infections in the Neonatal Period' to be published in the *Archives of Disease in Childhood.*

25. **Obituary:** The Executive has noted with profound regret the deaths of the following Honorary Members since the Association last met. Letters of sympathy have been sent on your behalf to the families concerned.

HONORARY MEMBERS: Thomas Barlow.
Edmund Cautley.
Humphry Rolleston.
Hugh Thursfield.

CORRESPONDING MEMBER: Joseph Brennemann.

26. **Resignations:** Resignations have been received from Dr. Norman Carmichael and Dr. Glen Davison.

Scientific proceedings (August 2, 1945):—

1. DR. J. L. HENDERSON (Edinburgh) (introduced by Prof. Charles McNeil): 'Statistics of prematurity.' A standardized method of presenting statistics on prematurity is an essential foundation for reliable scientific data regarding this serious paediatric problem. The figures of the large maternity hospitals and prematurity units are not comparable owing to the lack of a uniform method of statistical analysis. It is suggested that the following five conditions would provide a suitable comparative basis:—

(1). A large number of infants, preferably at least 500, as the proportion in the lighter weight groups is relatively small and figures relating to very small numbers are statistically insignificant.

(2). Accurate weighing at birth. The figures of large maternity hospitals only are reliable.

(3). Definition of the weight range of viable prematurity. The range suggested is 5½ lb. (2500 gm.) to 2¾ lb. (1250 gm.) inclusive. The upper limit of 5½ lb. has been universally adopted. The proposed lower limit of 2¾ lb. (Henderson, 1945, *J. Obstet. Gynaec.*, **52**, 29) has the following advantages:—(a) It corresponds approximately to the present standard of viability, i.e. an estimated gestation period of 28 weeks, the age at which the foetus is presumed to become viable. (b) It is the only round figure in the neighbourhood of 2 to 3 lb. at which exact correspondence of the avoirdupois and metric systems occurs. (c) The minimum weight is exactly half of the maximum weight, a desirable simplification. Infants weighing less than the minimum standard weight of 2¾ lb. should be classified as pre-viable (as at present by the 28 weeks standard) and placed in a separate category. In a series of 1670 liveborn premature infants, 8·3 per cent. were pre-viable.

(4). Subdivision of the standard weight range (5½ to 2¾ lb. incl.) into standard half-pound weight groups (5½ to 5 lb., 5 to 4½ lb., etc.). Subdivision is essential for comparative purposes as the proportion of larger and smaller premature infants varies in different series of cases.

(5). Segregation of 'booked' and 'unbooked' cases. 'Booked' refers to mothers who arrange their confinement in hospital early in pregnancy without recommendation, whereas 'unbooked' refers to mothers who are admitted as emergencies or are recommended for confinement in hospital because of ill health, obstetrical or otherwise, in the present or in a previous pregnancy. This condition is fundamental as the prognosis is much better in booked than in unbooked cases. Unbooked cases are not admitted to some maternity hospitals whereas in others they form a substantial minority of cases. In a series of 762 premature infants, 45 per cent. were born of booked mothers and 55 per cent. of unbooked mothers; the mortality rate was 15·1 per cent. in the booked cases and 37·2 per cent. in the unbooked cases.

2. DR. A. BARLOW (London) (introduced by Dr. D. Paterson): 'Prognosis in prematurity.' In a series of 514 premature infants (hospital 255, private 259) and 501 controls (hospital 149, private 352) it was found that 33·6 per cent. of the premature group and only 11·2 per cent. of the control group showed some form of mental abnormality.

TABLE 1

	Total	Normal	Mentally Abnormal	Per cent. Abnormal
Premature..	514	341	173	33
Control ..	501	445	56	11·2
Hospital prematures..	255	171	84	33
Private prematures..	259	170	89	34·3
Hospital controls..	149	127	22	14·7
Private controls ..	352	318	34	9·6

The hospital patients were taken from children attending the out-patient department at Great Ormond Street. The only selection involved was the exclusion of all cases under the age of six months. Apart from this, the cases were taken consecutively.

The abnormal group was composed of gross mental defects (45), mentally backward (53), epileptic (22), spastic (25), mongols (11), others (hydrocephalus, microcephalus, etc. (17). The incidence of mental abnormality increased with decreasing birth weight.

TABLE 2

Birth weight	Total	Normal	Abnormal	Per cent. Abnormal
Less than 2½ lb. ..	11	4	7	64
2½–3½ lb. ..	49	22	27	55
3½–4½ lb. ..	121	86	35	35
4½–5½ lb. ..	333	229	104	31·2
Totals ..	514	341	173	33·6

TABLE 3

Birth weight	Total	Normal	Abnormal	Per cent. Abnormal
5½–6½ lb. ..	121	107	14	11·6
6½–7½ lb. ..	184	164	20	10·8
7½–8½ lb. ..	130	115	15	11·5
Over 8½ lb.	66	59	7	10·6
Totals ..	501	445	56	11·2

If the cases are arranged under age groups, the proportion or mentally abnormal children is consistently higher in the premature series.

TABLE 4

Age	Prematures		Per cent. Abn.	Age	Controls		Per cent. Abn.
	Total	Abn.			Total	Abn.	
6/12–1 year	51	19	37	6/12–1 year	31	8	26
1–2 years	113	58	51	1–2 years	79	16	20
2–3 years	80	27	34	2–3 years	64	9	14
3–4 years	60	23	38	3–4 years	49	4	8
4–5 years	35	9	26	4–5 years	58	4	7
5–8 years	98	16	16	5–8 years	108	10	11
Over 8 years	77	21	27	Over 8 years	112	5	4·5

3. DR. G. DAVISON (Newcastle) (introduced by Prof. J. C. Spence): 'Statistics of pyloric stenosis.' A series of 500 consecutive cases of pyloric stenosis, treated at the Babies' Hospital, Newcastle-on-Tyne, between the years 1925 and 1943, was analysed after division into consecutive hundreds. Criteria of diagnosis were given, and evidence that the cases were unselected. The number of deaths fell steadily from 34 in the first hundred to four in the fifth. Consideration of figures for the average duration of symptoms, weight on admission, and loss of weight since birth, showed that the fall in mortality could not be attributed to earlier diagnosis; nor was it due to any increase in breast feeding. The increased use of surgery was a possible factor, the number of surgically treated cases rising from 76 in the first hundred to 95 in the last. Surgery was carried out under local anaesthesia in 46 of the first 76 cases, while open ether was the anaesthetic for the last 95—evidence that local anaesthesia is not necessary for safe surgery in pyloric stenosis. Intravenous 'drip' therapy was used first in case 206 and in 48 later cases; it was thought that this was an important factor in reduction of mortality. A factor not capable of analysis, but one thought probably to be the most important, was increasing skill on the part of the nursing staff. Evidence was given indicating that the incidence of pyloric stenosis in this country is in the region of 0·28 per cent. (±0·08 per cent.) of all live births, a figure not significantly different from that of 0·40 per cent. (±0·08 per cent.) given by Wallgren for Gothenberg.

4. PROF. A. E. NAISH (Sheffield): 'Congenital malformations of the heart associated with lower chest recession.' The mechanism of inspiratory recession of the lower chest, leading to a Harrison's sulcus, is inadequately understood. It is commonly attributed to ribs which are soft and yielding, combined perhaps with some obstruction to air entry. This is the explanation given when it is associated with rickets or prematurity. Eight cases of its association with congenital malformation of the heart are now brought forward. All were full term, of birth weights ranging from 6 lb. to 9 lb. 2 oz. None had had any trace of rickets. The recession seemed to have little connexion with the size of the heart since the 6-foot x-ray showed great variation in this respect. Half the cases had been seen shortly after birth and the recession was then well marked. One of these was only two days old. The association seems to be fairly common, since five out of the eight had been collected in the past six months. Such a clear-cut association seems to offer an opportunity for the investigation of the mechanism by which inspiratory recession is prevented in the normal infant.

5. DR. R. PUGH (London) (introduced by Dr. D. PATERSON): 'Preliminary observations on serum protein values in infancy.' An attempt was made to correlate certain clinical pictures including prematurity, congenital pyloric stenosis, coeliac disease and infantile diarrhoea with their associated protein depletion. Several cases were illustrated showing how the normal values may be restored by concentrated serum infusions and the type of distribution that ensues between tissue and circulation of fluids. Cases of congenital pyloric stenosis showing spontaneous degeneration of serum protein following operation and the retardation by an intercurrent infection were cited. The prevalence of a close association between low serum protein level and clinical oedema was observed, as was the normal range encountered in four cases of fibrocystic disease of the pancreas in spite of absence of pancreatic trypsin. The value of half-strength plasma transfusions in maintaining the protein nutrition in infantile diarrhoea was stressed along with some theoretical considerations involved.

6. DR. M. BODIAN (London) (introduced by Dr. D. Paterson): 'Penicillin, its dosage and administration in infants.' A series of 78 cases, under the age of one year (37 of which were neonates—under the age of one month) was treated with penicillin at the Hospital for Sick Children, Great Ormond Street. Staphylococcus aureus was responsible for the infections in 75 per cent. of all cases, and in 81 per cent. of the neonates. Penicillin is thus highly indicated in this group of infections. A dosage scheme of 1000 units per pound expected body weight per 24 hours is suggested. This is divided into six doses and each dose made up in 1 c.cm. normal saline given, every four hours intramuscularly. Average penicillin levels on this four-hourly dosage scheme were compared with those in adults on a comparable dosage given at

three-hourly intervals, and similar results were obtained. Levels were assessed three and four hours after an injection; they were still bacteriostatic in the majority of cases. Eighty-six per cent. of all bacteria other than gram-negative bacilli tested for penicillin sensitivity were susceptible to the average penicillin level obtained with this dosage. Threefold increase of dosage did not affect the issue materially.

7. Prof. J. C. Spence (Newcastle): 'An experiment in control of neo-natal infections in a maternity hospital.' The circumstances of war caused the evacuation of a maternity hospital to an old Victorian building hastily converted to its new purpose. Sanitary facilities were defective, and the pressure of work was heavy, including a high proportion of emergency and operative midwifery. Neo-natal infections and ward epidemics amongst the infants were frequent. Attempts to control these by bed spacing were not successful. In 1944 the experiment was started. From January to June, 1944, was used as a period of preliminary observation without alterations of existing conditions. In that period the infections continued. Detailed recording of every infective symptom was instituted. Out of 941 live births, 134 were premature infants and nursed in a special nursery and thereby excluded from the experiment. The remaining 807 infants were nursed and observed in the general maternity wards with their mothers. In this period there were 61 cases of severe infection, 42 of which were acutely ill and 14 of which died. After this preliminary period of observation and record the experiment was made of prohibiting all routine complementary fluid feeding thereby reducing the handling of the babies by nurses, and leaving other conditions unaltered. Complementary fluids were given in special cases (under 5 per cent. of total numbers of infants) and only on the prescription of the paediatric registrar. In the next six months' period (July to December, 1944) there were 952 live births (114 premature and excluded from the experiment) and of the 838 infants under observation in the wards there were five isolated cases of infective illness with two infant deaths one of which had also congenital heart disease and was much handled. The experiment was continued for a further period, i.e. January to June, 1945. In that period there were 786 live births (100 of which were premature and excluded from the experiment) and 686 retained in the wards under observation. Amongst them there were four isolated cases of infective illness with only one death, which was due to B. coli meningitis beginning within 24 hours of birth after difficult labour. An important procedure in the experiment was the use of an elaborate graphic ward chart with coloured symbols to denote each separate infective symptom as it arose. It is deduced from these results that the prohibition of complementary fluid feeding to new babies diminishes the chances of infective illnesses. The weight gain of infants was not adversely affected by withholding routine complementary feeding with water or saline mixtures. During the period of the experiment the infections amongst the premature infants in the special nursery were more frequent and more severe than amongst the infants nursed in the general wards.

8. Dr. D. W. Winnicott (London): 'The value of breast feeding (psychological).' A mother, in her total management of her infant, but especially in her feeding technique, is laying the foundation of her child's mental health. The value of actual breast feeding is to be found in the relative richness of detail in the physical relationship of infant and mother. These details of early experience are highly significant in the development of the personality. It is in respect of the infant's aggression that breast feeding is most obviously important. Excitement produces the urge to bite and destroy. To have not in fact destroyed the breast in a thousand feeds gives valuable reassurance to an infant. Add to this the tremendously powerful ideas that accompany instinctual experiences. For the mother the actual breast feeding, besides being infinitely pleasurable, increases her confidence in her body and her deeper self; it also gives reassurance to her in respect of her unconscious fear of being destroyed by her infant, this fear being a common cause of breast failure.

Friday, August 3, 1945:—

1. Dr. A. G. Watkins (Cardiff): 'Tuberculous infection in patients admitted to a general children's ward.' A survey was carried out for a five-year period, 1939–43, to determine the incidence of tuberculous infection in patients admitted to the children's wards at Llandough Hospital, Cardiff. Although a diagnosis of tuberculosis excluded admission to these wards, the incidence of active tuberculosis was found to be 2·6 per cent. Thus:—

Total number of patients admitted to wards	4896	
Total number of Mantoux tested (1 in 1000)	1249	
Number of positive reactors ..	281—22	per cent.
Number of negative reactors ..	968—78	,, ,,

Of 281 positive reactors:—

199 considered non-active tuberculosis
82 considered active tuberculosis

Total number of cases with active tuberculosis ..	127
postive Mantoux ..	82
negative Mantoux ..	9
not tested	36

Active cases equal 2·6 per cent. of total admissions.

Analysis of the 127 cases of active tuberculosis showed:—

Site	0–1 yr.	1–5 yr.	5–14 yr.	Total
Intrathoracic ..	17	12	23	52
Meningitis ..	1	18	11	30
Adenitis	1	8	12	21
Joints	0	5	4	9
Abdominal ..	0	2	5	7
Bony	1	3	2	6
Renal	0	0	2	2
	20	48	59	127

The presenting symptoms of the intrathoracic cases were as follows :—

	0–1 yr.	1–5 yr.	5–14 yr.	Total
Bronchitis ..	6	3	0	9
Pneumonia ..	4	1	3	8
Wasting	3	2	2	7
Enteritis	3	0	0	3
Prolapsed rectum	1	2	0	3
Conjunctivitis ..	0	1	1	2
Erythema nodosum	0	1	1	2
'P.U.O.'	0	0	2	2
Rheumatism ..	0	0	1	1
Impetigo	0	0	1	1
Pleural effusion ..	0	2	12	14
	17	12	23	52

Tables were also shown giving the age incidence of the Mantoux reaction and the radiological findings in the intrathoracic group.

The importance of carrying out a routine tuberculin skin test on all children, especially those under five years of age, as a means of detecting hidden active tuberculous infection was stressed.

2. Dr. F. J. Ford (Glasgow): 'Vitamin D treatment of rheumatoid arthritis.' The literature on the treatment of rheumatoid arthritis by high dosage of vitamin D was reviewed briefly and the safe dosage and dangers discussed. It was shown that, from experience in adults, the opinion of those who have tried it is rather conservative and that improvement tends to be subjective rather than objective. The clinical histories of two cases of rheumatoid arthritis in children were given and their

course discussed with charts of the temperature, pulse, weight, sedimentation rate, white cell count, and distribution of the disease in each. It was considered that in view of the improvement following adoption of this line of treatment, especially in the younger child who changed from a bedridden deformed creature to an active well-nourished girl within six months, further trial and investigation of the possibilities of vitamin D therapy was called for.

3. DR. W. SHELDON (London): 'Tuberculous rheumatism.' This condition was defined, and the clinical division of Poncet and Leriche into arthralgia, acute articular rheumatism, and chronic rheumatism was accepted. The clinical histories of six cases were presented; of these one belonged to the first group, four to the second group, and one to the third group. Reasons were given for thinking that these cases were not merely examples of streptococcal rheumatism complicated by tuberculosis. The view was expressed that rheumatic phenomena, although usually associated with haemolytic streptococcal infection, could occasionally be caused by other bacteria, including the tubercle bacillus.

4. DR. K. D. WILKINSON (Birmingham): 'The organization of out-patients in a children's hospital.' The out-patient room in the past has given the young physician opportunities to gain experience to become a sound, if rapid, diagnostician; to make contacts with the public and the general practitioner; and so to build up, not only his own reputation but his practice. The great disadvantage of the out-patient's room has always been that far too much work has tended to be imposed upon a popular, capable individual, until his out-patients' clinic has become a burden, if not a nightmare, to the conscientious physician. In the future efficiency in the out-patients' room must be secured by some of the following measures:—

First, the limitation of the number of cases that any one man is expected to see. Having carefully worked this out I consider a session of 2½ hours is the optimum length, and that during this session not more than fifteen cases should be seen. If at the same time undergraduate or post-undergraduate teaching is to take place, it may be necessary to restrict the number of cases still further.

Secondly, the planning of an out-patient department so that the waiting-room and the consulting-room are made as convenient as possible.

Thirdly, the provision of adequate assistance, nursing, medical (as registrars or house physicians), and clerical, stenographers for writing letters, making notes and conducting the follow-up of cases, will all add to the efficiency of a department and lessen the labour of the physician.

It is most important that careful planning should be undertaken in order to obviate the disadvantages and increase the advantages of such a department.

5. PROF. C. MCNEIL (Edinburgh): 'The clinical material of child health, where to get it and how to use it.' (see p. 151)

SCIENCE AND THE BRITISH MEDICAL ASSOCIATION.

The first of the two chief objects set out in the Memorandum of Association of the British Medical Association is the promotion of the medical and allied sciences, and it may fairly be said that pursuit of the second, namely the maintenance of the honour and interests of the medical profession, directly contributes to the attainment of the first. In the pursuit of its scientific activities, details of some of which are given below, the Association spends each year a considerable portion of its income.

Foremost amongst these activities is the publication of the *British Medical Journal*, with a weekly circulation of over 55,000 copies. The *Journal* serves as a comprehensive record of current developments and a forum for discussion in every field of medical science and professional organization in this country. The Association also publishes quarterly the following Specialist Journals : *British Heart Journal*, *British Journal of Industrial Medicine*, *Journal of Neurology and Psychiatry*, *Annals of the Rheumatic Diseases*. Apart from its periodical publications, the Association from time to time undertakes investigations, whether through special Committees or by the promotion of collective research, and publishes reports on the results. Recent examples of such reports are those on psycho-analysis, tests for drunkenness, mental deficiency, nutrition, fractures, relation of alcohol to road accidents, medical education, physical education, miners' nystagmus, etc. Copies of such reports can be obtained on application to the Secretary, B.M.A. House, Tavistock Square, W.C.1. Notices of investigations actually in progress are published from time to time in the *British Medical Journal*.

In the organization of the Scientific Sections at its Annual Meetings, the Association provides an unrivalled opportunity for discussion of new methods and old difficulties, not only within the confines of small groups of specialists but between specialists and the main body of the profession. British Medical Association Lectures in the Divisions and Branches afford another means of contact between the specialist and the general practitioner, and the regular clinical meetings and discussions arranged by many of the Divisions and Branches are an outstanding feature of the local life of the Association.

For many years the Association has offered Scholarships and Grants to the amount of £1,000 annually to enable approved workers to prosecute research in subjects of their own choice. Besides these annual grants, a number of special Prizes are awarded by the Association, e.g. the Stewart Prize for work on epidemic disease, the Middlemore Prize for work on a prescribed subject in some department of ophthalmic medicine or surgery, the Katherine Bishop Harman Prize for research in the disorders incident to maternity. These prizes are awarded periodically, and notice of pending awards is published in the *British Medical Journal* and elsewhere. In addition, the Association awards annually the Sir Charles Hastings Clinical Prize for systematic observation, research and record in general practice. Particulars of all prizes, scholarships and grants may be obtained on application to the Secretary.

Members are entitled to use the Reading Room at the House of the Association, with its files of periodical medical literature, British and foreign, the Reference Library, and the Circulating Library. The Librarian is always ready to answer enquiries by members, whether personal or postal, and to supply references.

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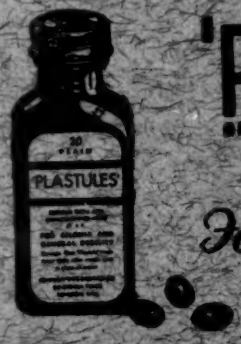

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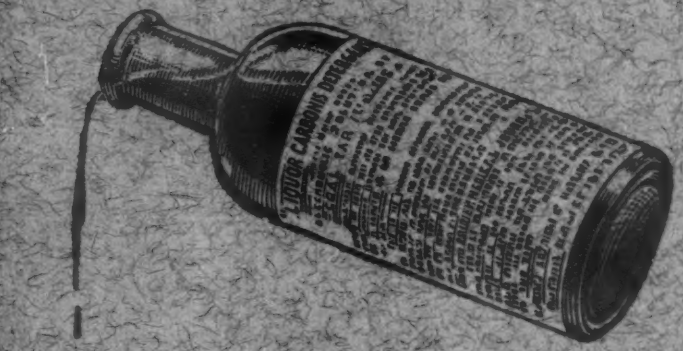

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IDEAL FOR TOILET AND NURSERY

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